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SKIN DISEASES AND SYPHILIS IN THE ENGLISH COLONIES OF NORTH AMERICA

WITH NOTES ON THE SUBSEQUENT PERIOD *

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Dermatosyphilology in the United States began to show signs of growth about the middle of the nineteenth century, and by 1871 its foliage was so luxuriant that White,[1] evidently thinking that there was need of pruning, said:

> Another new feature in the literature of cutaneous diseases is the publication of separate books on single affections. . . . Some of these have swollen to a monstrous size, and if pricked of their verbiage, personal conceit, and whims, and stripped of their ridiculously arbitrary and undemonstrated theories, would dwindle to the reasonable limits which a simple record of facts and justifiable deductions alone require.

This gentle judgment possibly may have given the inspiration to L. Duncan Buckley [2] for the motto "Brevity, indeed, upon some occasions, is a real excellence. Cicero, Brutus, 13, 50," which he, in 1874, chose for his *Archives of Dermatology*, which at that date became the successor of the *American Journal of Syphilography and Dermatology*.

The various phases of dermatosyphilology since the date referred to have been well covered by White [3] in his address on the History of the American Dermatological Association and in his editorial on "Modern Dermatology"; [4] by Ravogli [5] in his address on the history of the Section on Cutaneous Medicine of the American Medical Association; by

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* Read at the Meeting of The Beaumont Medical Club, Cromwell, Conn., Oct. 10, 1924.

1. W(hite), J. C.: Modern Dermatology, editorial, Am. J. M. Sc. **61**:466, 1871.

2. Buckley: Arch. Dermat. **1**:1, 1874.

3. White, J. C.: The president's address before the American Dermatological Association, J. Cutan. Dis. **15**:347, 1897.

4. W(hite), J. C.: Editorial, J. Cutan. Dis. **21**:1, 1903.

5. Ravogli, A.: Chairman's address, Section on Cutaneous Medicine and Surgery, J. A. M. A. **30**:813 (April 9) 1898.

Wende [6] in his "Review of Dermatological Journalism in the United States," and by Fox [7] in his address at the semicentennial of the New York Dermatological Society.

Before this time, dermatosyphilology did not exist as a specialty, and the intention here is to collect a few scattered notes of dermatologic interest from early writings.

The time under consideration is roughly divided into two periods, that before and that after 1800. At the beginning of the latter period, there was rapid progress in medicine, but until after the Revolution, American medical literature was practically nonexistent, and good physicians were few. On Feb. 20, 1721-1722, William Douglass [8] wrote from Boston to Cadwallader Colden:

> We abound with Practitioners, though no other graduate than myself, we have fourteen apothecary shops in Boston; all our Practitioners dispense their own medicines.

Douglass, whose clinical study of scarlet fever is "the first real important work on the disease," was a man of many activities, and Weaver,[9] in his delightful study of him, says that he "was the first really remarkable medical man of this country" and that "It is time that we should recognize him as a great man for any time and place, and should honor him for achievement accomplished under most adverse surroundings."

Systematic search for information on the subject here presented has not been made. Most of the information obtainable is found sparsely scattered in books of travel in the colonies, and in diaries, letters and records published by historical societies, and the little here collected has for the most part been found in casual reading.

Probably one of the most common dermatologic troubles was the mosquito bite, which to the newly arrived colonist and to the traveler was not the innocuous lesion it is to us. References to the tortures inflicted are frequent in books of travel in the colonies. Kalm,[10] writing from Philadelphia in 1748, said that when the mosquitoes were thick, people used smoke to keep them away. He describes his trials as follows:

> In day time or at night they come into the houses, and when the people are gone to bed they begin their disagreeable humming, approach always nearer to

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6. Wende, G. W.: A brief Historical Review of Dermatological Journalism in the United States, J. Cutan. Dis. **30**:389, 1912.

7. Fox, G. H.: Anniversary address at the semi-centennial celebration of the New York Dermatological Society, Arch. Dermat. & Syph. **1**:80 (Jan.) 1920.

8. Kittredge, G. L.: Letters of Samuel Lee and Samuel Sewell, etc., Pub. Colonial Soc. of Mass. **14**:159, 1912.

9. Weaver, G. H.: Life and Writings of William Douglass, M.D., Bull. Soc. Med. Hist. Chicago **2**:229-251, 1921.

10. Kalm, Peter: Travels into North America, etc., trans. into English by John Reinold Forster, Warrington, William Eyres **1**:144, 1777.

the bed, and at last suck up so much blood, that they can hardly fly away. Their bite causes blisters in people of delicate complexion. . . . In *Sweden* I never felt any other inconvenience from their sting, than a little itching, whilst they sucked. But when they stung me here at night, my face was so disfigured by little red spots and blisters, that I was almost ashamed to show myself.

Schoepf [11] referred to the susceptibility of the newcomers, saying that:

A sound European constitution soon accustoms itself to all the inclemencies of the climate, so that most of the patients in the hospitals are usually recruits. One fact is worthy of mention in this connection, which perhaps testifies as forcibly as anything can to the need of acclimatization, and is moreover universally admitted to be true. In a new-comer, almost every bite of the mosquito (*Culex pipiens*, L.) produces a boil during the first year after his arrival, but fails to have this effect in the subsequent years.

The facts stated in this observation of Schoepf's were described again about a hundred years later in a paper by White,[12] who studied the reaction of mosquito bites in a family of six who had come from England and who had been in Boston only two weeks. The lesions in these cases started as erythema and went through the stages of papule, vesicle, pustule, furuncle or wheal or bleb, and in some instances there were large bullae which were so generally distributed on the affected areas as to give an appearance of pemphigus of extreme grade. He also brought out the point that in the case of bedbug and flea bites, the reaction of those unaccustomed to them was frequently marked, but that when the person becomes accustomed to the bites, only the small lesions with which we are all acquainted develop on him.

All sorts of other insect pests are also referred to frequently. Of North Carolina, Brickell [13] says:

The louse is not plenty in this province. They are eaten by Rusticks for the *Jaundice*, and *Consumption*, and to provoke urine.

Of fleas Kalm [14] said:

I have seen them on the grey squirrels, and on the hares which have been killed in such desert parts of this country, where no human creature ever lived. As I afterwards came further up into the country, and was obliged to lie at night in the huts of the *Indians*, I was so plagued by immense quantities of fleas, that I imagined I was put to the torture. They drove me from the bed, and I was very glad to sleep on the benches below the roof of the huts.

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11. Schoepf, Johann David: The Climate and Diseases of America, trans. by J. R. Chadwick, Boston, 1875, p. 22. (Original published in Ertangen in 1781.)

12. White, J. C.: On the Protection Acquired by the Human Skin and Other Tissues Against the Action of Certain Animal Poisons After Repeated Inoculations, Boston M. & S. J. **8**:297, 1871.

13. Brickell, John: The Natural History of North Carolina, etc., Dublin, 1737, p. 165. (Reprinted and edited by J. B. Grimes, no date.)

14. Kalm, P.: Footnote 10, **2**:9.

Brickell [15] said:

The *Fleas* are very plenty in some parts of this Province, especially in those places where the *Indians* dress their Deer Skins, they have no Physical Virtues yet known, but are certainly most troublesome guests. They are generated by Dust, as also of putrefied Sweat, and are destroyed by Decoctions made of *Coloquintida.*

He [16] also found a therapeutic use for black flies:

The large *Black-Mackrel-Flies* are also plenty, especially in the *Summer* time, and are the same as those with us in *Europe.* The powder of these *Insects* and their juice cures Baldness.

Gnats: [17]

Punchins, as the *Dutch* call them, are the little gnats (*Cimex pulicaris,* Linn) which abound here. They are very minute, and their wings grey, with black spots. They are ten times worse than the larger ones, or muskitoes; for their size renders them next to imperceptible; they are everywhere careless of their lives, suck their fill of blood, and cause a burning pain.

Bedbugs, too, were encountered: [18]

Bugs (*Cimex lectularius*) are very plentiful here. I have been sufficiently tormented by them, in many places in *Canada*: But I do not remember having seen any with the *Indians,* during may stay at *Fort Frederic.*

Schoepf [19] mentioned another pest:

People working in these forests (North Carolina) during the summer find the wood-louse (Ticks, Seed-ticks, *Acarus americanus,* L) a great plague, at many times and places very numerous. Their bite causes great pain and wicked boils; with their probiscis they bore deep into the skin, and when they have become fast lodged, must be probed out, if possible.

Poison ivy and its allies were early acquaintances of the colonists. Kalm [20] noted that they affect some and not others:

. . . The face, the hands, and frequently the whole body swells excessively, and is affected with a very acute pain. Sometimes bladders or blisters arise in great plenty, and make the sick person look as if he were infected with a leprosy. In some people the external thin skin, or cuticle, peels off in a few days, as is the case when a person has scalded or burnt any part of his body. . . . Their eyes are sometimes shut up for one, or two and more days together by the swelling. . . . I have known old people who were more afraid of this tree than of a viper; and I was acquainted with a person who merely by the noxious

15. Brickell, J.: Footnote 13, p. 165.
16. Brickell, J.: Footnote 13, p. 160.
17. Kalm, P.: Footnote 10 **2**:296.
18. Kalm, P.: Footnote 10 **2**:11.
19. Schoepf, Johann David: Travels in the Confederation, 1783-1784, trans. and ed. by A. J. Morrison, Philadelphia **2**:106, 1911.
20. Kalm, P.: Footnote 10, p. 77.

exhalations of it was swelled to such a degree, that he was stiff as a log of wood, and could only be turned about in sheets.

Later, he [21] tried experiments on himself with one of the plants, after which he said:

I have not experienced anything more of the effects of this plant, nor had I any desire so to do.

Eruptions caused by bad food were described by Schoepf: [22]

In the item of fish, there are said to have been disagreeable occurrences here (i.e., Charleston) (although more rarely), such as have been remarked here and there in other regions of North America. That is to say, certain fish, otherwise of sound and edible species, seem at times from some unknown cause to have injurious, almost poisonous properties. Several instances of this sort happened during my stay in Rhode Island, in the summer of 1779. In the family of a Jew, by the name of Meyer, a seaperch (*Percae* species) was got ready for the table, this being commonly one of the best and most gustable fishes of those waters. A short time after the meal was over most of the family, but especially those who had eaten of the liver of the fish, were seized with giddiness, headache, nausea, and gripings, with some fever. A sort of rash appeared on the skin, and the outer skin peeled. . . . The inhabitants of Rhode Island know of a good many such instances.

Prickly heat was apparently not well known in Europe at this time. Of it Schoepf [23] said:

A peculiar kind of eruption, if it may be so called, known by the name of the "prickling heat" is almost universal here in summer. The skin is covered with a quantity of large or small red spots that are occasionally attended by a disagreeable itching sensation, from which symptom the name is derived. The spots are not raised, but come and go with the increase or decrease of the heat. People who keep in-doors do not have them so often, or to so marked a degree, as those who are exposed to the sun. On my own person I have observed them during the midday hours, most commonly after having been out; my entire skin would then be red. When the weather begins to moderate this eruption disappears, and the skin desquamates almost imperceptibly. The common people, who are universally disposed to regard every eruption as healthy, look upon "prickling Heat" in the same way, and therefore consider its sudden subsidence to be injurious; it is not so, however, except in so far as this action is attended by the suppression of evaporation. The whole appearance is nothing more than a greater determination of the red blood to the vessels of the skin, when they are relaxed by the heat from without. The rays of the sun are often powerful enough to raise vesicles on the tender parts of the body when exposed.

Brickell [24] also noted that: *"Rashes* and *Prickley-heat* are Common Disorders here," and that: [25]

21. Kalm, P.: Footnote 10, p. 80.
22. Schoepf, J. D.: Footnote 19, p. 190.
23. Schoepf: Footnote 11, p. 14.
24. Brickell, J.: Footnote 13, p. 49.
25. Brickell, J.: Footnote 13, p. 50.

Tetters and *Ring-worms* are common in this Province, and are easily cur'd by several Plants in this Country, and especially by the juice of the Sheep-Sorrel, by applying it to the Part infected.

Several herbs acquired the name of cancer root from the virtues which they were supposed to possess in the cure of this disease, and naturally cancer quacks flourished here at this time, as they have flourished in every time and in every place. One of the best known of them [26] was:

. . . a certain Martin, who boasted of possessing an all-powerful but secret cure for cancer. This aroused the credulity and won the confidence of his people so much the more because of the clever pretext that the discovery of the root (according to him the medicine came from a root) had been communicated to him in confidence by an old Indian at Pittsburg. Although shrewd and impartial physicians at Philadelphia found good reason to doubt the highly praised worth of the remedy in genuine cases of cancer, the incredible number of imaginary or pretended cases of the disease, news of which came in from all parts, was astonishing. Never before had so much been heard of this malady. But it was certain that fear and prepossession caused the anxious patient to fancy every obstinate or rooted impostume must be cancerous, and it was to be expected of the purveyor of the famous remedy that he, for his advantage, should claim everything to be cancer and thus multiply his cures. However it was by no means clearly made out that the medicine used by him was in reality taken from nothing but a root. But he sought to spread abroad this belief, and almost every year made a journey to Pittsburg pretending to dig his mysterious root there from a particular hill on the Monongahela.

After Martin's death, Dr. Rush [27] showed that the active ingredient of this powder was arsenic. He closed his paper with these words:

I flatter myself that I shall be excused in giving this detail of a *quack* medicine, when the Society reflects, that it was from the inventions and temerity of quacks, that physicians have derived some of their most active and useful medicines.

In those days as now it was easy for the cancer quack to get testimonials:

Signed by six fools of different sorts
All cured of Cancers made of warts.[28]

The hopelessness of cure even by the best therapy of the time was described by Tennant: [29]

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26. Schoepf, J. D.: Footnote 19, p. 287.

27. Rush, Benj.: An Account of the Late Dr. Hugh Martin's Cancer Powder, with Brief Observations on Cancers, Tr. Am. Philosophical Soc. **2**:212, 1786.

28. Hopkins, Lemuel: Epitaph on a patient killed by a Cancer-Quack, in Smith, Elihu H.: American Poems, Litchfield **1**:137, 1793; Arch. Dermat. & Syph. **6**:187, 1922.

29. Tennant, J.: Every Man his own *Doctor* or The Poor Planter's Physician, Ed. 2, Williamsburg and Annapolis, W. Parks, 1734, p. 52.

Cancer. Another woful Case, is, a Cancer, which some despairingly imagine to be incurable; tho; blessed be God, there have been some Instances of Success, by the Method hereafter mentioned. In the meantime, it usually begins with little hard Lumps, or Swellings, in the Breast, Lip, or other glandulous Part of the Body. These afterwards break into painful sores, which eat farther and farther, 'til at last, they reach some Vessel, or Mortal Part.

In this Case, the Patient must submit, in the first Place, to have the hard Lump cut clean out, as soon as he is convinced it is a *Cancer.* And for curing the Wound, he can't do better than make use of the following *Balsam.* He must boil 6 Ounces of *Sassafras Root,* and as much *Dogwood Root,* in a *Gallon* of *Water,* 'til it be wasted to a *Pint,* and having strained it off, must drench a *Pledget* therein, and apply it warm to the Sore, renewing it every Day. And if he will have the Patience to continue this for some Time, I can assure him, he will not be the first that has been blessed with *Success.*

Let him drink *Sassafras* Tea every Morning, live temperately, upon light and innocent Food, and abstain intirely from strong liquor. The Way to prevent this Calamity is, to be very sparing in eating Pork, to forbear all salt, and high season'd Meats, and live chiefly upon the Garden, the Orchard, and the Hen-house.

Scabies was probably a common affliction, for Schoepf [30] collected the names of a dozen native plants that were sometimes used in its treatment. Sulphur was of course also used. Then, as now, it kept the patient busy. Joshua Hempstead,[31] in his diary on the date of Sept. 19, 1730, says: "I was at home all day. I keep house, have been daubing with Brimstone for ye Itch."

Among other skin diseases for which native plants were used are most of the commoner ones: ivy poisoning, the exanthemas, variola, aphthae, paronychia, burns, ulcerations, ulcerated breasts, impetigo, tinea, erysipelas, shingles, herpes, pernio, corns, warts and hypertrichosis.[30] Sneeze root (*Helenium autumnale*) was used as a hair dye. "Folia contrita succum nigrum praebent, quo ad capillos tingendos utuntur nonnulli." [32]

In the medical literature of this time, the theory is constantly expressed that many diseases, including syphilis and most skin diseases, are caused by eating pork. Schoepf [33] wrote as follows concerning this belief:

Despite all that has been said about the injurious effect of pork,— which may have been the reason of its having been forbidden by the Mosaic Law—in this army, notwithstanding the constant consumption of salt pork, no ill effects have

30. Schoepf, Johann David: Materia Medica Americana Potissimum Regni Vegetabilis. Erlangae Sumptibus 10. Iac. Palmii, 1787. (Reprinted in the Bulletin of the Lloyd Library, 1903, Bulletin No. 6) passim.

31. New London County Historical Society Collections **1**:226. (Reference supplied by Dr. C. B. Graves, New London.)

32. Schoepf: Footnote 30, p. 125.

33. Schoepf: Footnote 11, p. 19.

been observed, and moreover scarcely anything is known of the common skin diseases which used to be laid to its account; when affections of the skin have occurred, they have invariably been produced and kept up by neglect of external cleanliness.

In the literature of the colonial period, there are many references to syphilis, but as a rule they contain little accurate information. It is frequently spoken of as a variety of yaws. Fox [34] gives Wood as the authority for the statement that: "The first authentic reference to yaws in American literature is to be found in a volume by Brickell on the Natural History of North Carolina, etc., published in 1737." Brickell's [35] statement, quoted by Fox, is similar to one made by Lawson in 1714. In fact, Brickell has been charged with largely plagiarizing Lawson, and Weeks' explanation that these charges are only partially correct "and do grave injustice to Brickell," [36] does not well satisfy, for many passages, even in his preface, have been copied almost literally from Lawson.

Lawson's [37] statement in regard to yaws is:

At these cabins came to visit us the king of the Santee nation. He brought with him their chief doctor, or physician, who was warmly and neatly clad with a match coat, made of turkies feathers, which makes a pretty show, seeming as if it was a garment of the deepest silk shag. This doctor had the misfortune to lose his nose by the pox, which disease the Indians often get by the English traders that use amongst them; not but the natives of America have for many ages (by their own confession) been afflicted with a distemper much like the lues venerea, which hath all the symptoms of the pox, being different in this only, for I never could learn, that this country distemper, or yawes, is begun or continued with gonorrhea, yet it is attended with nocturnal pains in the limbs, and commonly makes such a progress as to vent part of the matter by boils, and several ulcers in the body, and other parts, oftentimes death ensuing. I have known mercurial unguents and remedies work a cure, following the same methods as in pox, several white people, but chiefly the Criolos, losing their palates and noses by this devouring vulture.

It is epidemical, visiting these parts of America which is often occasioned through the immoderate drinking of rum, by those that commonly drink water at other times. Cold night's lodging, and bad open houses, and more chiefly, by often wetting the feet and eating such quantities of pork as they do, which is a gross food, and a great propagator of such juices as it often meets withal in human bodies, once tainted with this malady, which may differently (in some respects) act its tragedy, the change being occasioned by the difference of climates and bodies as in Europe.

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34. Fox, Howard: The Prevalence of Yaws (Frambesia tropica) in the United States, Arch. Dermat. & Syph. **6**:657 (Dec.) 1922.

35. Brickell, J.: Footnote 13, p. 48.

36. Brickell, J.: Footnote 13 (introductory note by J. B. Grimes).

37. Lawson, John: The History of Carolina, etc., London, 1714. Reprinted, Raleigh, 1860, pp. 37-38.

In fact, there are many references to yaws in the colonies before that made by Brickell. Rev. John Clayton,[38] in 1687, referring to Virginia, wrote to Dr. Nehemiah Grew of London as follows:

> Among the Indians they have a Distemper which they call Yaws, which is nearly related to the French-Pox; which they are said to cure with an Herb that fluxes them. But this I have only by Hear-say.

And Tennant,[39] in 1734, said:

> The Pox may be cured exactly in the same Manner: And because the Symptoms are much the same, it is very probable, the one was a Graft of the other (i.e., Yaws).

Another reference to yaws, preceding that of Brickell, will be found below in the item from the Barbados Gazette of 1733-1734.

The belief that yaws and syphilis were different varieties of the same disease persisted for a long time. Plenk,[40] in 1787, said:

> The venereal poison seems to be a degenerated form of the disease which is known in America under the name of yaws, which in the Antilles seems to be chiefly an endemic disease.

Jonathan Hutchinson,[41] even after the discovery of the spirochete of syphilis and of that of yaws, still questioned whether "this syphiloid be not syphilis itself in a variant form."

The first known outbreak of syphilis in New England occurred in 1646. John Winthrop,[42] in his Diary said: "There fell out a loathsome disease at Boston, which raised a scandal upon town and country, though without just cause."

Faith in mysterious cures, especially Indian cures for syphilis, was unbounded at this time, as the following quotations will demonstrate:

> *Barbados.*[43] We have had lately from *South Carolina* the following Recipe, as an effectual Cure for all Distemper arising from an inveterate Scurvy, and for the *Yaws*, Lame-Distemper, Pox, &c., for the Discovery whereof, a Negro-Man in *Virginia* was freed by the Government, and had a Pension of Thirty Pounds Stirling settled on him During his Life. (The recipe is then given.)

Cotton Mather [38] wrote to the Royal Society in 1712:

> We have had a sort of *Cranes-bill*, which differs little from yours; except perhaps in the Colour of ye *Flowre*, which with us is of sky-blue, and the large-

38. Kittredge, G. L.: Footnote 8, p. 186.

39. Tennant, J.: Footnote 29, p. 50.

40. Plenk, J. J.: Lehre von den Venerischen Krankheiten, Ed. 2, Vienna, 1787, p. 14.

41. Hutchinson, Jonathan: Syphilis, New Edition, New York, 1910, p. 544.

42. Lane, J. E.: A Few Early Notes on Syphilis in the English Colonies of North America, Arch. Dermat. & Syph. **2**:215 (Aug.) 1920.

43. Barbados Gazette, Jan. 2, 1733, in Caribbeana **1**:258, 1741. (Reference supplied by Prof. G. L. Kittredge, Harvard University.)

ness of ye *Root* which is near that of *Ginger*. Our Indians call it by the name of *Tauttipang*; and from them we learn the manner, and strange effect of using it. It is an Infallible cure, and *safely*, and *Quickly*, and easily performs it, for that filthy Disease (the Lues Venera) which the just Judgment of God had reserved for our later Ages, wherein so many Fools abandon themselves to the destructive Debaucheries of Unchastity.

Kalm [44] has a variation of the same story:

. . . and the venereal disease is common here. The *Indians* are likewise infected with it; and many of them have had it; and some still have it; but they likewise are perfectly possessed of the art of curing it. There are examples of *Frenchmen* and *Indians*, infected all over the body with this disease, who have been radically and perfectly cured by the *Indians*, within five or six months. The *French* have not been able to find this remedy out; though they know that the *Indians* employ no mercury, but that their chief remedies are roots, which are unknown to the *French*. I have afterwards heard what these plants were, and given an account of them at large to the Royal *Swedish* academy of sciences.

The Rev. Andrew Burnaby,[45] while stopping at Winchester, Va., heard that there was not far away, "A Medicinal spring, specific in venereal cases," and "A spring of a Sulphureous nature, an infallible cure for particular cutaneous disorders."

John Bartram [46] described lobelia for syphilis, having learned the secret from "the learned *Peter Kalm* (who gained the knowledge of it from Colonel *Johnson*, who learned it from the *Indians*, who, after great Rewards bestowed on several of them, revealed the Secret to him.)"

And Carver said: [47]

It has long been a subject of dispute, on what continent the venereal disease first received its destructive power. This dreadful malady is supposed to have originated in America, but the literary contest still remains undecided; to give some elucidation to it I shall remark, that as I could not discover the least traces among the Naudowessies, with whom I resided so long, and was also informed that it was yet unknown among the more western nations, I think I may venture to pronounce that it had not its origin in North-America. Those nations that have any communication with the Europeans, or the southern tribes, are greatly afflicted with it; but they have all of them acquired a knowledge of such certain and expeditious remedies, that the communication is not attended with any dangerous consequences.

Lawson [48] also told of "admirable cures" by the savages, but in his description of the results of the cure on physician and patient, there

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44. Kalm: Footnote 10 **3**:33.

45. Burnaby, Andrew: Travels Through the Middle Settlements of North America in the Years 1759 and 1760, London, T. Payne, 1775, p. 35.

46. Lane, J. E.: Footnote 42, p. 219.

47. Carver, Jonathan: Three Years Travels Through the Interior Parts of North America (1766-1768), Philadelphia, Joseph Cruikshank, 1789, p. 200. (The first edition was printed in 1778.)

48. Lawson, John: Footnote 37, pp. 39-40.

seems to be a small joker attached. The doctor is the "chief doctor" referred to above, who was brought along by the "king of the Santee nation."

> Now to return to our doctor, who, in the time of his affliction, withdrew himself (with one that labored under the same distemper) into the woods. These two perfected their cures by proper vegetables, &c., of which they have plenty, and are well acquainted with their specific virtue.
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> I have seen such admirable cures performed by these savages, which would puzzle a great many graduate practitioners to trace their steps in healing, with the same expedition, ease and success; using no racking instruments in their chirurgy, nor nice rules of diet, and physic, to verify the saying, *qui medice vivit, misere vivit.* In wounds which penetrate deep and seem mortal, they order a spare diet, with drinking fountain water; if they perceive a white matter or pus to arise, they let the patient more at large, and presently cure him.
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> After these two had performed their cures at no easier rate than the expense of both their noses, coming again amongst their old acquaintance so disfigured, the Indians admired to see them metamorphosed after that manner, enquired of them where they had been all that time, and what were become of their noses?

Schoepf [30] collected ten or a dozen different native plants used by the Indians or colonists for syphilis, and in another place,[49] in a few sentences summed up the whole matter of the Indian cures for the disease.

> Of the medical knowledge of the Indians, the opinion here and there in America is still very high. The greater number, but not the well-informed, are convinced that the Indians, mysteriously skilled in many excellent remedies, carefully and jealously conceal them from the white Europeans. As always, so here, people are deceived by the fancy that behind a veil of mystery there lie hidden great and powerful things. I see no reason to expect anything extraordinary or important, and I am almost certain that with the passage of time nothing will be brought to light, if as is the case, outright specifics are looked for and presumable infallible remedies. . . . Most of the diseases for the healing of which the skill of the Indians is especially praised are simple, those in which nature may work actively and effect the most salutory changes. . . . The observers and panegyrists of the so much belauded Indian methods of therapy are commonly ignorant people who find things and circumstances wonderful because they cannot offer explanations from general principles. . . .

The foregoing notes show the extremely modest beginnings of dermatosyphilology. In contrast to these modest beginnings, and before leaving this period, a word must be said in regard to the first dermatosyphilologist, whose light for a few moments brightly flashed in the medical darkness of the colonies. I refer to Daniel Turner,[50] whose interest in the "good literature and liberal arts and sciences" that were

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49. Schoepf, J. D.: Footnote 19, p. 284.

50. Lane, J. E.: Daniel Turner and the first degree of Doctor of Medicine conferred in the English Colonies of North America by Yale College in 1723, Ann. M. Hist. **2**:367, 1919.

flourishing here, led him to "adorn the Republic of Letters, wherever established" by sending some books to strengthen "the infantile state" of the library of the "College of the Academy of Yale."

In return for his gift he received from this institution, in 1723, the honorary degree of Doctor of Medicine, in compliance with a hint dropped in the postscript to his letter accompanying the books:

> If your worships consider me worthy of the doctoral degree of Yale Academy and have the diploma sent to me, I shall receive it not only as a sign of your gratitude, but I shall consider it an honor as much as though it had been conferred by another university, though of greater note. Farewell most learned sirs and may your academy flourish.

Thus a dermatosyphilologist received the first degree of M.D., given by an educational institution in this country. However, it is only fair to state that some wag of the time, whose identity I have failed to discover, interpreted the M.D. as *multum donavit.*

The second period, which is now to be considered, was much less primitive. Scientific medicine began here and there to show signs of growth, but dermatosyphilologic literature is almost nil and may be covered by a few illustrations. Until 1800, practically no books were found in the colonies except imported English works. From the number of editions, and the frequency with which copies are at present found in old book stores, we may easily infer that Turner's books on dermatology and syphilis were popular here.

In 1788, a translation of the third edition of Swediaur, "Practical Observations on the more obstinate and inveterate Venereal Complaints," was published in New York, and his "Complete Treatise on the symptoms, effects, nature and treatment of Syphilis," in Philadelphia, in 1815.

In "Dr. Lyman Spalding," that delightful biography and picture of medical life in New England in the early part of the nineteenth century, by Dr. James A. Spalding,[51] is described Spalding's attempt to publish an American edition of Willan in 1806-1807. He gave up the attempt because of his failure to find anyone who could satisfactorily reproduce the illustrations in colors. He had plates made by Alexander Anderson, but Anderson could not print them, and he tried David Edwin, whose impressions were pale and indistinct. He then tried James Akin, who was no more successful.

Thus the publication had to be abandoned, and all that remains of the American edition as planned by him, are two very rare and probably unique impressions of Plate IX, Figs. 1 and 2; of Lepra Alphos and Lepra Nigricans, pulled from the plate engraved by Dr. Alexander

51. Spalding, J. A.: Dr. Lyman Spalding, the originator of the United States Pharmacopoeia, etc., Boston, W. M. Leonard, 1916, pp. 126-130.

Anderson. A pale, pinkish impression is the one pulled by David Edwin; a dark, brownish one represents "the experiment made by James Akin."

These two impressions are still in the possesion of Dr. James A. Spalding,[52] of Portland, Me. One of them "is pasted into an album backing up a diploma for a Grand Lodge of Masons."

Spalding[53] was apparently much interested in diseases of the skin, for after his failure he wrote to Alibert in 1808, and received from him one of his works, which he started to translate. This translation was not finished.

Not much later, American editions of English authors and translations of French authors began to appear.

Bateman's "Synopsis" was published in Philadelphia in 1818 and again in 1824.

Cazenave and Schedel's work was translated and published in 1829, 1832, 1846 and 1852.

An edition of Samuel Plumbe appeared in 1837; of Jonathan Green in 1838 and 1839; there were at least half a dozen editions of Erasmus Wilson, the first in 1843; Rayer in 1845; Neligan in 1852, and Hillier in 1865 and 1868.

Occasional articles on dermatosyphilology began to appear about 1800. In 1805, John Douglass wrote "An experimental essay on mercury."

In the same year, Joseph Klapp wrote:

> A chemico-physiological essay, disproving the existence of an aeriform function in the skin, and pointing out, by experiment the impropriety of ascribing absorption to the external surface of the human body.

In 1806, J. Tongue wrote:

> An inaugural dissertation upon the three following subjects: 1. An attempt to prove that the lues venerea was not introduced into Europe from America; 2. An experimental inquiry into the modus operandi of mercury in curing the lues venerea; 3. Experimental proofs that the lues venerea and gonorrhea are two distinct forms of disease.

Toward the latter end of this period, Silas Durkee produced several publications: "A case of erythema tuberculatum et oedematosum"; in 1859,[54] "A Treatise on Gonorrhea and Syphilis"; and in 1868, "Contributions to Dermatology; eczema, impetigo, scabies, ecthyma, rupia, lupus." A second edition of the last was printed two years later.

At this time, too, students began more frequently to go to Europe for study, and a few dermatologic articles appeared from their pens in German journals.

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52. Spalding, J. A.: Personal communication, Sept. 15, 1919.
53. Spalding, J. A.: Footnote 51, p. 148.
54. Durkee, S.: A Case of Erythema, Tuberculatum et Oedematosum, Boston M. & S. J. **54**:189 (April) 1856.

In 1868, David Haight [55] published an article on "Vesicle Formation in Some Diseases of the Skin"; William Young [56] on "Anatomy of the Edematous Skin"; W. H. Giddings,[57] "On the Anatomy of Lupus Erythematosus"; John Collins Warren,[58] "On Keloid"; and in 1869, Richard Derby [59] published one, "On the Anatomy of Prurigo."

American books on dermatology now began to appear. In 1868, H. F. Damon published his "Neuroses of the Skin: their pathology and treatment"; and in 1869, "The Structural Lesions of the Skin; their pathology and treatment."

F. D. Weisse [60] said of Damon's work:

> There will be two more volumes to complete the work. It is Doctor Damon, to whom we shall be endebted for the first American treatise on diseases of the skin; up to the present time our dermatological literature was composed of American traditions and translations.

This paper may well be brought to an end by quoting Walsh's [61] résumé of the end of this period and the beginning of the next one.

> In dermatology New York holds a particularly high place in the development of the specialty, because members of the New York medical profession were pioneers in the making of history in many regards not alone for this country but for the world. It was in New York City in 1869 that the first association of physicians with interests exclusively dermatological, was established. Seven years later, in connection with the Centennial Medical Congress in 1876, the call for the organization of the American Dermatological Association was made from New York. This was the first national association in dermatology founded anywhere in the world, and held its first formal meeting at Niagara Falls in September, 1877.
>
> For a generation before this, New York had been a leader in interest in dermatology. The first dispensary in America for the treatment of skin and venereal diseases was the Broome Street Infirmary for Diseases of the Skin, established in New York City in 1836 by Drs. Henry D. Bulkley and John Watson. At this infirmary, the year of its foundation, Dr. Bulkley, who had made special studies in skin and venereal diseases at the St. Louis Hospital, Paris, gave a course of seven lectures illustrated by clinical cases, the first lectures of the kind in the country. Five years later he delivered a course of lec-

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55. Haight, David: Ueber Blasenbildung bei einigen Hautkrankheiten, Sitzungsb. d. k. Akad. d. Wissensch. Math.-Naturw. **57,** April, 1868.

56. Young, William: Zur Anatomie der ödematösen Haut, Sitzungsb. d. k. Akad. d. Wissensch. Math.-Naturw. **57:** 1868.

57. Geddings, W. H.: Zur Anatomie des Lupus Erythematosus, Sitzungsb. d. k. Akad. d. Wissensch. Math.-Naturw. **57,** March, 1868.

58. Warren, J. C.: Ueber Keloid, Sitzungsb. d. k. Akad. d. Wissensch. Math.-Naturw. **57,** March, 1868.

59. Derby, Richard: Zur Anatomie von Prurigo, Sitzungsb. d. k. Akad. d. Wissensch. Math.-Naturw. **59,** February, 1869.

60. Weisse, F. D.: Letter to Doyon in Ann. de dermat. et syph. **2**:75, 1870.

61. Walsh, James J.: History of Medicine in New York **1**:213-214, 1919.

tures to the medical students of the College of Physicians and Surgeons in New York in the spring time. The first professorship in the subject was established in New York City at New York University in 1867.

After this the development of dermatology as a specialty was rapid and thorough. During the decade between 1860 and 1870 most of the dispensaries of New York City established dermatological clinics, and practitioners of medicine began to recognize the necessity for having special information with regard to skin diseases. The first systematic treatise on dermatology by an American author was "An Elementary Treatise on Diseases of the Skin," by Dr. Henry G. Piffard, of New York, which was published in 1876. This anticipated by a year the textbook of "Practical Treatise on Diseases of the Skin," by Dr. Duhring of Philadelphia. The first Journal devoted to skin diseases, exclusively, was the *American Journal of Syphilography and Dermatology,* edited by Dr. Morris H. Henry, of New York. The first number of this periodical appeared in January, 1870, and it was discontinued in 1874, only to be succeeded that same year by the quarterly Journal, *Archives of Dermatology,* with Dr. L. D. Bulkley as the editor. The *Archives* continued its publication for some eight years until it was succeeded in 1882 by the *Journal of Cutaneous and Venereal Diseases,* the original editors of which were Henry G. Piffard and Prince A. Morrow.

The first hospital for diseases of the skin in America was the New York Skin and Cancer Hospital, opened for patients January 1, 1883. As some three thousand patients were treated during the first three years, the need of such an institution became very clear.

THE WASSERMANN TEST*

XIV. THE EFFECT OF SULPHARSPHENAMIN ON THE WASSERMANN REACTION

DAVID L. BELDING, M.D.

BOSTON

This paper is the fourth of a series dealing with the effect of certain antisyphilitic remedies on the Wassermann reaction. It describes the action of sulpharsphenamin—an arsphenamin derivative which differs from neo-arsphenamin by the presence of an additional atom of oxygen in each side chain—on the Wassermann reaction in congenital and acquired syphilis. The principal preparations used were manufactured by the Laboratorie de biochémie médicale of Paris and the Massachusetts Department of Public Health.

In order to obtain the uncomplicated effect of sulpharsphenamin on the Wassermann reaction, no auxiliary drugs such as mercury and the iodids have been used. Since mercury itself influences the reaction and only one course of sulpharsphenamin was administered, our results should prove less favorable than if several courses of combined antisyphilitic treatment had been employed.

The strength of the Wassermann reaction was measured as described in a previous paper [1] before, half way through and one week after treatment, and at monthly intervals over a period of five months after treatment. For observing the effect of drug therapy, the quantitative method of determining the strength of the Wassermann antibody possesses certain advantages over the ordinary Wassermann test. It gives a more exact record of the serologic changes in the individual patient, whereas the latter records only the negative or weakly positive and fails to measure the strongly positive reactions, which on our arbitrary scale range from 4 to 256 units.

The drug was administered intravenously in a freshly prepared 10 per cent. solution and intramuscularly or subcutaneously in a 20 per cent. solution. The dosage was determined by weight, the standard being the equvalent of 0.9 gm. for a 68 kg. patient, which is the commonly accepted maximum dose of neo-arsphenamin. Children were treated three times a week and adults one to two times over a period of from four to six weeks, the number of injections ranging from four to twelve. Patients with congenital syphilis received only intramuscular treatment; those with acquired syphilis, intravenous or intramuscular treatment.

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* From the Evans Memorial and Boston University School of Medicine.

1. Belding, D. L., and Holmes, R. H.: Wassermann Test; Effect of Mercurosal on Wassermann Reaction, Arch. Dermat. & Syph. **9**:459 (April) 1924.

Since the publication of a previous paper [2] concerning the toxic effects of sulpharsphenamin, further subcutaneous injections of a 30 per cent. solution have been given. Several patients individually received four different commercial preparations. Little difference in toxicity was observed. The injections were fairly well tolerated, the local reaction depending on the size of the dose, the individual injection and the sensitiveness of the patient. Although results with particular lots as well as preparations of sulpharsphenamin undoubtedly differ, owing to the variable factors of patient and technic, it seems impossible to differentiate by clinical observation minor differences in local toxicity. In our hands, the subcutaneous administration in the arm produced more or less induration and an occasional impairment of motion, and as a rule was less satisfactory than intramuscular administration.

Clinical results with these patients were fully as good as with arsphenamin. All patients with active syphilis showed general improvement. Secondary and tertiary lesions disappeared rapidly. The prompt healing of tertiary ulcers and skin lesions was especially noticeable, although the high rate of dosage may have accelerated this process.

PATIENTS

Table 1 gives a clinical classification of the groups represented in this study. The children who ranged from 15 months to 16 years in age had strongly positive Wassermann reactions, but few signs of active syphilis. In addition to the tabulated data, practically all had enlarged glands, five showed irregular or enlarged hearts, and four a lack of nervous control. Eighteen received the French and two the Massachusetts sulpharsphenamin. The majority had received more or less previous treatment with arsphenamin and mercury, and two groups had received within the past six months treatment with mercurosal and neo-arsphenamin. With two exceptions, a uniform weekly and total dosage of 1.7 to 2 times the maximum dose of neo-arsphenamin per kilogram of body weight was administered in three injections weekly over a period of four weeks. Except for one patient, comparatively slight ill effects resulted from this high dosage, in contrast with more noticeable toxic conditions in adult patients. Evidently children are able to assimilate proportionately larger doses of sulpharsphenamin than adults. The adult patients, ranging from 16 to 60 years, were more or less representative of the types of chronic and active syphilis encountered in an outpatient clinic.

The terms ex-primary, ex-secondary, etc., refer to patients who once had symptoms of these stages but no longer show clinical evidence of

2. Belding, D. L.: Wassermann Test; Sulpharsphenamin in Treatment of Syphilis, Arch. Dermat. & Syph. **9**:470 (April) 1924.

syphilis. The classification "latent" signifies serum-positive syphilis with no history or clinical signs of the disease.

NEGATIVE WASSERMANN REACTION

A negative Wassermann reaction as reported here refers to the results of several tests and does not depend on a single negative, which

TABLE 1.—*Clinical Classification of Patients*

	Children,	Adults								
	Congenital	Secondary	Active Tertiary	Ex-primary	Ex-secondary	Ex-tertiary	Neurosyphilis	Congenital	Latent	Total
Previous Symptoms:										
None	7	3	4	..	..	..	..	..	10	17
Chancre	..	2	1	5	..	..	3	..	..	11
Chancre and secondary skin lesions	..	..	..	1	..	..	..	..	..	1
Chancre and iritis	..	..	..	1	..	..	..	..	..	1
Chancre, secondary skin lesions and iritis	..	1	..	..	..	..	..	..	..	1
Chancre and tertiary skin lesions	..	..	1	1	..	..	..	..	..	2
Chancre, secondary skin lesions and bone	..	..	1	..	..	..	..	..	..	1
Secondary skin lesions	..	..	..	..	1	..	..	..	..	1
Secondary mucous membrane lesions	..	..	..	..	1	..	..	..	..	1
Secondary skin and mucous membrane lesions	..	..	..	..	1	..	..	..	..	1
Secondary skin and tertiary palate lesions	..	..	..	..	..	..	1	..	..	1
Tertiary skin lesions	..	..	1	..	..	..	1	..	..	2
Tertiary ulcer	..	..	..	..	..	2	1	..	..	3
Congenital skin lesions	6	..	..	..	..	..	..	..	..	..
Congenital skin and snuffles	2	..	..	..	..	..	..	..	..	..
Bone and joint	..	..	..	..	..	1	..	..	..	1
Bone, joint and skin	1	..	..	..	..	..	..	..	..	..
Bone, joint and interstitial keratitis	1	..	..	..	..	..	..	..	..	..
Interstitial keratitis	3	..	..	..	..	..	..	..	..	..
Interstitial keratitis and teeth	..	..	..	..	..	..	..	1	..	1
Interstitial keratitis, teeth and bone	..	..	..	..	..	..	..	1	..	1
Bone	..	..	..	..	..	2	..	..	..	2
Neurosyphilis	..	..	1	..	..	..	..	..	..	1
Total	20	6	9	8	3	5	6	2	10	49
Present Symptoms:										
Chancre and secondary skin	..	1	..	..	..	..	..	..	..	1
Secondary skin	..	3	..	..	..	..	..	..	..	3
Secondary skin and mucous membrane	..	2	..	..	..	..	..	..	..	2
Tertiary skin	..	..	4	..	..	..	..	..	..	4
Tertiary skin and tabes	..	..	1	..	..	..	..	..	..	1
Tertiary ulcer	..	..	2	..	..	..	..	..	..	2
Gumma of liver	..	..	1	..	..	..	..	..	..	1
Bone	1	..	1	..	..	..	..	..	..	1
Neurosyphilis, advanced	..	..	..	..	..	..	6	..	..	6
Hutchinson teeth	5	..	..	..	..	..	..	2	..	2
Bone development	6	..	..	..	..	..	..	..	..	..
"Saddle" nose	1	..	..	..	..	..	..	..	..	..
Liver, enlarged	1	..	..	..	..	..	..	..	..	..
Interstitial keratitis	1	..	..	..	..	..	..	..	..	..
"Snuff" fundi and old iritis	1	..	..	..	..	..	..	..	..	..
"Snuff" fundi and teeth	1	..	..	..	..	..	..	..	..	..
"Snuff" fundi and "saddle" nose	1	..	..	..	..	..	..	..	..	..
"Snuff" fundi and enlarged liver	1	..	..	..	..	..	..	..	..	..
Total	19	6	9	..	..	..	6	2	..	23

at times may occur in a slightly positive serum through variations in laboratory technic. It represents the ordinarily accepted Wassermann negative, whereas the quantitative method, which is used in the remainder of this paper, gives a more delicate measurement on the negative side.

The influence of sulpharsphenamin on the Wassermann reaction has been reported by eleven investigators in connection with clinical observa-

tions. The two largest series, by Doble [3] and Duroeux,[4] deal chiefly with patients with early syphilis. The relatively few cases reported by other investigators are distributed over different stages of the disease.

Children.—Boone and Weech [5] obtained a negative reaction in 55 per cent. of twenty-one children under 1 year old with active congenital syphilis after six injections of sulpharsphenamin followed by mercury. Crawford and Fleming [6] obtained 39 per cent. of negative reactions in children under 1 year, and none in older children. Papegaaij and Rinsema [7] found no diminution in the reaction in a few children with congenital syphilis. In our series of twenty children over 1 year old, the greater part of whom had received previous treatment, two negative and two doubtful reactions were obtained.

Adults.—Duroeux, in a series of 124 intensively treated cases, obtained 87 per cent. negative reactions after one course of treatment and 100 per cent. before the completion of the second. In 162 cases, in which the patients received longer but less intensive treatment, 68 per cent. became negative after the first course, 87 after the second, and 100 after the third. Doble obtained a negative reaction in 87.5 per cent. of 230 patients after one course. Our figures for secondary syphilis, 100 per cent., coincide with their results, which evidently are based on cases of early syphilis. Our figures for old cases of syphilis agree substantially with the slight response shown by the patients cited in the literature, which give 19 per cent. for tertiary and 8 per cent. for neurosyphilis. Nine of the forty-nine adults who previous to treatment had borderline positive reactions, below 4 units on our quantitative scale, were discarded, since the occurrence of a negative in such cases does not give reliable information as to the effect of treatment. Of the remaining forty so-called strong positives, from 4 to 128 units, thirteen were negative six months after treatment. Many of these patients did not have negative reactions until some weeks after treatment (Table 2), and the negative reactions which occurred before the eighth week were in patients with secondary syphilis.

Owing to a variation in the initial strength of the reaction, the previous treatment and the stage of the disease, the production of a negative Wassermann reaction is of questionable value for the comparison of the therapeutic efficiency of antisyphilitic drugs unless

3. Doble, F. C.: Lancet **1**:70 (Jan. 13) 1923.

4. Duroeux, L.: Progrès méd. **36**:155 (April 9) 1921.

5. Boone, F. H., and Weech, A. A.: Treatment of Early Hereditary Syphilis with Intramuscular Injections of Sulpharsphenamin, Am. J. Dis. Child. **27**:39 (Jan.) 1924.

6. Crawford, E., and Fleming, G. B.: Lancet **2**:700 (Oct. 1) 1921.

7. Papegaaij, J., and Rinsema, P. G.: Acta derm. ven. **2**:149, 1921.

comparable groups of patients are selected. Table 2 illustrates the influence of these factors.

Initial Strength of Reaction.—A serum with a low initial reaction tends to become negative sooner than one with a strong initial reaction. None of the children with an initial reaction over 16 units attained a negative. The adults with above 16 units had but one-third the chance of those with weaker reactions to attain a negative reaction. The adults whose reactions became negative had an average initial reaction of 12 units. Patients with a reaction above 16 units who have received previous treatment with arsphenamin have relatively little chance of attaining a negative reaction after one course of sulpharsphenamin.

TABLE 2.—*Production of a Negative Wassermann Reaction*

	Children		Adults	
	Total Number of Cases	Percentage Negative	Total Number of Cases	Percentage Negative
Total number of cases	20	10	40	33
Initial strength of reaction:				
32 to 128 units	11	0	7	14
4 to 16 units	9	22	33	36
Previous arsphenamin treatment	13	8	26	27
No previous treatment	7	14	14	43
Duration of disease:				
1. Under 4 years: Untreated	1	0	6	83
Treated	3	0	8	25
Total	4	0	14	43
2. Over 4 years: Untreated	6	17	8	50
Treated	10	10	18	11
Total	16	13	26	23
After sulpharsphenamin treatment:				
1 week	20	0	40	5
4 weeks	20	0	40	10
8 weeks	20	0	40	20
12 weeks	20	0	40	25
20 weeks	20	10	40	33

Previous Treatment.—The adult patients who had received previous treatment with arsphenamin gave a lower percentage of negative reactions than the untreated patients (Table 2), in spite of the advantage of the low average initial strength of 16 units as compared with 33 for the untreated. As shown later, the production of a negative depends to some extent on the character of the previous treatment.

Stage of Syphilis.—The stage of the disease is a most important factor in the production of a negative reaction. In acquired syphilis of less than four years' duration, half of the cases became negative as compared with a quarter in syphilis of more than four years' duration (Table 2). The reaction became negative in all our patients with secondary syphilis, in about half of the patients with active tertiary syphilis and in only 11 per cent. of those with latent syphilis and neurosyphilis. In therapeutic and clinical comparisons between miscellaneous groups of patients, due consideration must be given to the rapid disappearance of the reaction in early syphilis.

REDUCTION OF THE WASSERMANN ANTIBODY

Our statistics demonstrate that if the production of a negative Wassermann reaction is used as a therapeutic index for antisyphilitic drugs, it is of value only when large numbers of patients in the same stage of the disease are compared. Quantitative measurements that take into consideration the actual strength of the reaction provide a more accurate means of comparing small numbers, but, owing to technical difficulties and individual variation in the patients, only gross differences in the effect of drugs can be detected.

TABLE 3.—*Effect of Sulpharsphenamin on the Wassermann Reaction in Congenital Syphilis*

	Number of Cases	Unit Value of Wassermann Antibody Before Treatment	Fall in Wassermann Reaction: Weeks After Start of Treatment								
			0	2	5	7	9	11	13	17	30
Total cases	20	25.8	100	86	56	55	57	55	51	54	44
Stigmas	10	19.1	100	90	61	63	63	70	67	75	65
No stigmas	10	32.4	100	82	52	47	50	40	35	32	23
Symptoms	13	25.5	100	88	52	55	57	52	47	48	40
No symptoms	7	26.3	100	82	64	54	54	61	57	64	51
Poor nutrition	8	23.5	100	93	61	55	61	58	55	61	49
Good nutrition	12	27.3	100	81	53	54	53	53	48	48	41
Over 5 years	12	26.0	100	86	54	55	55	59	56	61	50
Under 5 years	8	25.5	100	86	60	54	59	50	43	43	34
Previous treatment:											
Arsphenamin	7	24.0	100	99	57	61	71	71	67	81	64
Arsphenamin and mercury	6	21.8	100	72	53	51	39	47	47	45	43
Mercury	3	40.0	100	96	44	44	61	51	44	34	24
None	4	26.7	100	75	69	56	53	41	33	33	26
Total arsphenamin and mercury	13	23.0	100	87	55	57	56	61	59	66	54
Total mercury and none	7	30.8	100	84	58	51	57	46	38	34	25
Comparison with previous mercury in same patients:											
Mercury	5	52.0	100	—	75	—	65	—	45	50	65
Sulpharsphenamin	5	26.2	100	80	40	43	48	48	43	32	28
Comparison with previous intramuscular neo-arsphenamin in same patients:											
Neo-arsphenamin	6	53.3	100	83	48	—	48	—	33	—	—
Sulpharsphenamin	6	25.3	100	99	58	62	75	67	61	78	58

Tables 3 and 4 show the reduction in the Wassermann antibody during and after treatment expressed in per cent., 100 representing the average strength previous to treatment. In our series, a reduction of 52 to 56 per cent. was obtained after a single course of sulpharsphenamin. In the average case, the effect was delayed, the maximum reduction being obtained in adults twenty weeks after treatment had ceased. This fact should be taken into consideration by persons using the Wassermann test as a therapeutic index, especially in comparing the efficiency of the various arsenical preparations. In early congenital syphilis, the reaction is readily influenced by treatment, but in the older cases, such as comprise our series, it is most resistant.

In clinical observations it is impossible to obtain the definite and exact conditions of animal experimentation, particularly as regards the control of variables, which tend to confuse the interpretation of experimental data. In all clinical comparisons of the effect of antisyphilitic treatment, due allowance must be made for such factors as: (1) individual variation, (2) duration of the disease, (3) amount of previous treatment and (4) rate of dosage.

Individual Variation.—Men as well as laboratory animals exhibit individual variations in the production of immune substances and in response to treatment. Certain syphilitic patients show no change in the Wassermann antibody titer under intensive and prolonged treatment, others respond at first but for long periods maintain a moderate or low titer before eventually becoming negative, and still others show a comparatively rapid reduction. In our series, three children showed a final strength less than 10 per cent. of the initial reaction, eight between 10 and 30 per cent., five around 50 per cent., and four no change. The adult patients in Table 4 fall into three groups: (1) 27 per cent. with a marked reduction, (2) 42 per cent. with a moderate reduction of three-fifths the original strength, and (3) 31 per cent. with no change in the Wassermann antibody.

The extent of reduction in the average case depends on the initial strength of the reaction, although the individual may show marked variation. The higher titer cases as a rule show more rapid and extensive reduction. Above 8 units, the reduction is over two-thirds, below this figure, about one-third. Although previous treatment with arsphenamin is largely responsible for this difference, the initial strength of the reaction is also a factor. The high titer, previously treated cases give a reduction of 70 per cent. as compared with 34 per cent. for the low, while the untreated cases show little difference, from 77 to 70 per cent. between the high and low groups. It is evident, especially in patients who have received previous arsphenamin treatment, that only patients whose serums contained the same amount of Wasserman antibody are suitable for serologic study as to the comparative results of different therapeutic agents.

Clinical Syphilis.—In the average case of active syphilis, a strongly positive Wassermann reaction usually accompanies clinical symptoms. The individual patient may vary from this standard. A negative reaction may be present with clinical symptoms, and strongly positive reactions are often found without clinical manifestation of the disease. As a rule, the average reaction in untreated syphilis is strongest during the latter part of the active secondary stage. Usually, the disappearance of clinical syphilis is followed synchronously or later by the reduction of the Wassermann reaction. As the disease becomes chronic, the

TABLE 4.—*Effect of Sulpharsphenamin on the Wassermann Reaction in Adult Patients with Syphilis*

	Number of Cases	Fall in Wassermann Reaction: Before Treatment	Half way Through Treatment	Weeks after Treatment: 1	4	8	12	16	20	24	Percentage of Maximum Neoarsphenamin Dosage: Total Dosage	Weekly Rate	Unit Value of Wassermann Antibody before Treatment
Total number of cases..	49	100	87	72	67	63	60	52	46	48	82	76	17.4
Individual variation													
No reduction.....	15	100	100	99	103	103	107	100	90	95	77	69	5.6
Moderate reduction...	21	100	88	74	65	62	54	45	43	40	101	81	28.8
Marked reduction.....	13	100	73	36	28	18	17	10	7	5	66	82	12.5
Initial Strength of Wassermann antibody													
1 to 8 units.....	32	100	94	80	78	75	74	65	57	59	75	73	5.1
16 to 128 units.....	17	100	71	57	46	39	34	28	26	26	93	80	40.5
Clinical syphilis													
1. Duration of disease													
(1) Under 4 years													
Untreated.....	6	100	71	45	20	16	14	10	10	10	78	81	18.0
Treated.....	11	100	84	73	73	68	65	51	33	36	75	63	8.8
Total.....	17	100	80	69	54	49	47	37	25	27	76	69	12.1
(2) Over 4 years													
Untreated.....	10	100	87	62	59	56	48	39	36	35	93	91	35.9
Treated.....	22	100	94	83	80	77	75	70	68	69	81	74	13.1
Total.....	32	100	92	77	73	70	67	60	58	58	84	79	20.2
2. Stages of disease													
(1) Secondary													
Untreated.....	4	100	56	18	5	2	2	2	2	2	74	73	15.0
Treated.....	2	100	100	50	38	10	6	5	4	4	111	119	16.0
Total.....	6	100	71	29	15	5	3	3	3	3	86	88	15.3
(2) Active tertiary													
Untreated.....	7	100	86	48	48	46	39	36	34	33	81	87	45.0
Treated.....	2	100	75	75	63	57	52	52	51	51	106	83	10.0
Total.....	9	100	84	54	51	48	42	40	38	37	86	86	37.2
(3) Latent													
Untreated.....	4	100	92	108	75	72	61	38	33	33	107	107	19.5
Treated.....	6	100	75	71	79	69	55	51	51	51	87	91	8.3
Total.....	10	100	82	86	77	70	57	46	44	44	95	97	12.8
(4) Neuro													
Untreated.....	1	100	100	50	50	38	38	38	38	38	113	62	16.0
Treated.....	5	100	100	100	93	93	93	83	73	83	77	63	3.4
Total.....	6	100	100	92	86	84	84	76	67	76	83	63	5.5
(5) Ex-syphilis, treated													
Ex-primary.....	8	100	91	69	82	82	88	69	59	58	84	82	7.6
Ex-secondary...	3	100	100	100	83	83	83	83	58	58	35	28	5.3
Ex-tertiary.....	5	100	93	87	85	77	76	70	60	64	85	71	10.8
Total.....	16	100	96	80	84	81	83	72	59	60	75	68	8.2
(6) Congenital, treated.....	2	100	75	79	46	63	63	63	63	63	51	35	67.0
Previous treatment with arsphenamin													
1. Untreated													
Intramuscular..	4	100	75	42	32	28	15	15	15	15	59	55	35.5
Intravenous (selected).....	4	100	56	17	13	11	12	12	12	12	83	101	46.0
Intravenous....	12	100	83	60	48	45	42	32	30	31	97	98	27.1
Total.....	16	100	81	56	44	41	35	28	26	26	87	87	29.2
2. Treated													
Intramuscular..	16	100	91	88	88	79	77	74	65	65	58	46	15.1
Intravenous....	17	100	84	74	76	71	69	55	49	50	100	92	8.5
1-5 gm. arsphenamin.....	16	100	81	69	65	60	58	53	50	50	80	74	10.7
5-12 gm. arsphenamin.....	14	100	96	95	96	92	90	78	64	68	79	70	5.2
Total.....	33	100	88	79	77	74	72	64	57	58	79	70	11.7
3. Duration of syphilis before treatment													
Less than 1 year	11	100	84	73	73	68	65	51	33	36	75	63	8.8
6-28 years.....	19	100	90	86	83	80	78	72	70	71	82	78	7.8
Intramuscular vs. intravenous													
Intravenous.....	29	100	88	67	63	59	56	45	41	42	98	95	16.2
Intravenous (selected)	20	100	90	67	66	61	62	48	44	43	96	95	17.9
Intramuscular.....	20	100	88	79	72	69	65	62	55	55	58	48	19.2

TABLE 4.—*Effect of Sulpharsphenamin on the Wassermann Reaction in Adult Patients with Syphilis—(Continued)*

	Number of Cases	Fall in Wassermann Reaction: Before Treatment	Halfway Through Treatment	Weeks after Treatment: 1	4	8	12	16	20	24	Percentage of Maximum Neo-arsphenamin Dosage: Total Dosage	Weekly Rate	Unit Value of Wassermann Antibody before Treatment
Sulpharsphenamin treatment													
1. Total dosage													
(1) Over ¾ maximum neo-arsphenamin dose													
Untreated	11	100	81	60	46	43	39	31	29	29	100	106	16.8
Treated	16	100	95	77	80	72	72	60	53	56	108	100	8.1
Total	27	100	89	70	66	60	59	48	43	45	105	103	11.6
(2) ¼–¾ maximum neo-arsphenamin dose													
Untreated	5	100	80	48	40	37	27	22	19	19	59	41	56.4
Treated	17	100	87	82	75	76	71	71	59	59	51	42	15.0
Total	22	100	85	74	67	67	61	60	50	50	53	42	24.4
2. Weekly rate													
(1) Over ¾ maximum neo-arsphenamin dose													
Untreated	9	100	82	67	50	48	43	33	31	31	101	115	18.3
Treated	13	100	97	72	76	65	67	51	47	47	109	111	10.1
Total	22	100	91	70	66	58	57	44	41	41	105	113	13.5
(2) ¼–¾ maximum neo-arsphenamin dose													
Untreated	7	100	78	42	36	32	25	21	19	19	70	51	43.1
Treated	20	100	86	84	79	80	75	72	62	65	59	44	12.7
Total	27	100	84	73	68	67	62	59	51	53	62	46	20.6
3. Toxicity													
Toxic symptoms	14	100	105	74	71	62	62	47	42	42	112	118	13.1
Nontoxic	15	100	71	60	55	56	51	45	40	42	85	74	19.1

reaction tends to lose its strength, except when the liver, spleen and vascular system are involved, and may become negative.

The response of the adult patient to treatment varies with the stage and duration of the disease. Table 4 gives a comparison between the response of patients with early and late syphilis. Patients with syphilis of less than four years' duration are more responsive to treatment with sulpharsphenamin than are those with older cases—both those who have had previous treatment and those who have not. In the early untreated cases, the reaction presents a particularly rapid fall during and immediately after treatment. In Table 3, children averaging 3.3 years showed a greater response to treatment than those averaging 10 years, although the initial strength of the reaction was the same in both groups. Children, in whom clinical lesions were detected prior to four months after birth, also showed a more marked response.

Patients with secondary syphilis, untreated or relapsing after insufficient treatment, gave the most rapid and pronounced response, the maximum reduction being attained four weeks after treatment. No difference in the active tertiary and the latent was noted in the previously untreated patients. In the treated patients, no difference was noted between the active tertiary, latent, ex-primary, ex-secondary or

ex-tertiary. Patients with neurosyphilis apparently responded less favorably to treatment, although the cases are too few to warrant any conclusion.

Active syphilis usually signifies recent syphilis, and consequently is more amenable to treatment. Excluding neurosyphilis and congenital syphilis, our adult patients with active syphilis responded to treatment more readily than those with inactive (with a history of previous clinical syphilis) and latent syphilis, giving a reduction of 77 as compared with 46 per cent. This difference is increased by the large proportion of patients with inactive syphilis who had received previous treatment and by those with active secondary syphilis who responded readily to treatment. If patients afflicted with syphilis of the same duration beyond the secondary stage with and without active clinical manifestations are compared, there is little difference in the response to sulpharsphenamin.

Children with signs of congenital syphilis were less responsive to treatment. Even eliminating the influence of previous treatment and difference in strength of the reaction, which may have influenced this result, it was still evident that patients with latent cases with no stigmas gave a more decided response. Little difference was observed between the children who had past or present clinical symptoms and those with no symptoms, but the lack of response in the latter was due to the inclusion of three children from one family, all of whom were resistant to treatment. In children who fell appreciably below the normal standard of nutrition, the response to treatment was slightly less marked than in those showing normal nutrition.

Changes in the Wassermann antibody may or may not coincide with clinical improvement. One child who had no clinical symptoms except skin lesions when 3 weeks old and who had received considerable mercury but practically no arsphenamin showed no clinical evidence of syphilis, except enlarged glands, at the beginning and the end of treatment with sulpharsphenamin. The Wassermann antibody fell under treatment from 24 to 8 units, and eventually became negative under treatment with mercury, but eight weeks after treatment, the patient developed a unilateral interstitial keratitis, no evidence of which had been observed by careful eye examination at the beginning and close of treatment. This case represents either the accidental development of clinical symptoms in a patient with serum positive congenital syphilis in spite of treatment, or more probably the activation of a latent process by sulpharsphenamin. Halloran [8] describes a somewhat similar case of iritis occurring under sulpharsphenamin treatment. Another child had an extensive ulceration and gumma of the left humerus which showed improvement but did not completely heal, although the Wassermann antibody was reduced from 32 to 8 units.

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8. Halloran, R. D.: Boston M. & S. J. **190**:55 (Jan. 10) 1924.

Previous Treatment.—Our statistics demonstrate that previous arsphenamin treatment has considerable influence on the response to sulpharsphenamin, and support the claims of the syphilologists who maintain that clinical experience demonstrates the existence of a treatment-fast condition. They also indicate that prolonged treatment with the arsphenamins serologically may not give as favorable results as varied or mixed treatment. The possibility of unconsciously selecting abnormally resistant persons among the previously treated patients, to some extent may augment the difference between the treated and untreated.

Certain patients respond readily to a small amount of treatment; others prove resistant even to strenuous and prolonged treatment. This treatment-fast condition is more marked in patients who have received previous treatment, only 6 per cent. of the untreated adults showing no change as compared with 43 per cent. of those previously treated. Three of the four Wassermann-fast children came from the same family.

Table 3 shows that children who had received an appreciable amount of arsphenamin with or without mercury responded less favorably to sulpharsphenamin treatment than children who had received no treatment or mercury alone. Little difference is noticeable between children who had received mercury and those who had received no previous treatment. From the standpoint of treatment within the past year the same observation holds true; children who had received neo-arsphenamin or arsphenamin recently did not respond as readily as those who had received only mercury or no treatment.

Adult patients who had received no treatment showed nearly twice the reduction of those previously treated. The strength of the Wassermann antibody before treatment with sulpharsphenamin in the average patient who had received previous treatment with arsphenamin was about two fifths of the untreated. The patients who received more extensive treatment with arsphenamin gave a smaller initial reaction and were somewhat less responsive to sulpharsphenamin than those who had received slight treatment. Either the low Wassermann antibody in these cases represents a resistant fraction more difficult to influence by treatment, or an arsphenamin-fast state may have been produced. Although in untreated cases a low antibody content is slightly more resistant than a high, the results are more suggestive of an arsphenamin-fast condition.

Patients previously treated with arsphenamin early in the disease responded more readily to treatment with sulpharsphenamin. The amount of previous treatment and the initial units were about equal in those treated within the first four years of the disease and those treated after six years or more. The early treatment in the first group aborted or retarded the disease, whereas in the second the disease was well estab-

lished before treatment. In these groups, the comparative response to sulpharsphenamin and to previous treatment is actually that of early and late syphilis. The time interval between the previous treatment and the sulpharsphenamin treatment had no apparent effect on the action of the latter.

Although our method is incapable of detecting minor differences, the results indicate that sulpharsphenamin has no marked advantage over arsphenamin in the reduction of these treatment-fast cases. It would seem that this type of arsenical preparation does not offer a radical enough change to offset a treatment-fast condition for an arsenical drug, although in some cases it may prove effective. From a serologic standpoint, we may conclude that a changing drug therapy is of greater value than long drawn out treatment with one preparation, that intensive treatment for a short period is preferable, that we must employ a different type of drug to obtain the best results, and that while neoarsphenamin and sulpharsphenamin may offer some change from arsphenamin treatment, the change is not radical enough to be thoroughly effective.

Sulpharsphenamin Treatment.—Our figures for total dosage and weekly rate are expressed in percentage of the maximum standard neo-arsphenamin dose of 0.0792 gm. per kilogram of body weight, comparable to six injections of 0.9 gm. in five weeks for a 68 kg. patient, and 0.0158 gm. per kilogram of body weight per week. The cases fall into two groups: (1) those receiving over three-quarters the maximum dose of neo-arsphenamin, and (2) those receiving from one-quarter to three-quarters. The former averages approximately the full and the latter about one-half the maximum dose.

Table 4 shows little difference in the reduction of the Wassermann antibody in these two groups. This observation holds true for the total dosage for both untreated and treated cases. The weekly rate, however, favors the higher dosage, suggesting that the intensity of the treatment rather than the total amount of sulpharsphenamin is the more important factor. Previously treated patients, who are more resistant to treatment, respond better to intensive treatment at a higher weekly rate, whereas untreated patients, who respond more readily to treatment with sulpharsphenamin, show no difference between the high and low dosage. The effect of treatment is not associated with the tolerance of the patient or with saturation by the drug. A comparison between patients receiving intravenous treatment who gave toxic symptoms in the form of peripheral neuritis and dermatitis and those who gave no toxic symptoms shows no difference in the reduction of the Wassermann antibody.

In untreated cases, serologic response appears as marked at one-half as at the full maximum dose. The rapid response to a small amount of sulpharsphenamin in the secondary cases is especially noteworthy. The

many instances of relapse after little treatment in early syphilis warn us that the smaller dosage may be insufficient to eradicate the disease. The clinician should remember that treatment sufficient to bring about a negative reaction in early syphilis by no means is sufficient to sterilize the patient, effect a cure or to prevent a relapse, and that in this respect a negative reaction is an untrustworthy criterion of cure.

Intravenous vs. Intramuscular Injection.—The difficulty in comparing the serologic results of intramuscular and intravenous treatment lies in the selection of comparable cases and the difference in dosage. By selecting twenty of the intravenous cases which were comparable to a similar number of intramuscular, the results were slightly in favor of the intravenous. There was no noticeable difference in the untreated patients, among whom were many with early syphilis, who respond readily to a small dosage. In the previously treated patients, those treated intramuscularly (Table 4) did not give as favorable a response as those treated intravenously, who received the maximum dosage, about twice that of the intramuscular.

In spite of the unfavorable results in those who have received previous treatment, it seems logical that intramuscular injections of sulpharsphenamin should prove of greater value than intravenous. The drug thus administered gives less systemic reactions and is more slowly excreted. In addition, it produces locally a nonspecific reaction which possibly stimulates the defensive mechanism of the body. With children, for whom the dosage is relatively small, it appears the method of choice over the intravenous.

Mercury, Neo-arsphenamin and Sulpharsphenamin.—Table 3 records the individual action of intramuscular injection of mercury and neo-arsphenamin compared with subsequent treatment with sulpharsphenamin in the same children. Comparison between the results of treatment with mercury and treatment with sulpharsphenamin gives a fairly representative picture of the effect of these drugs on the Wassermann antibody, since mercury, a different type, does not produce an arsphenamin-fast condition. The higher initial value of the Wassermann antibody favored the mercury group, yet the results with sulpharsphenamin were more pronounced. Treatment with mercury failed to produce a permanent reduction of the Wassermann antibody, as is shown by the partial recovery, whereas the sulpharsphenamin treatment maintained its gain except for minor irregularities due to technical errors.

The comparison between intramuscular injection of neo-arsphenamin and sulpharsphenamin is unsatisfactory, as an arsphenamin-fast condition renders patients less amenable to treatment with sulpharsphenamin. For this reason, no comparison can be made, since it would be mani-

festly unfair to conclude that sulpharsphenamin was less efficient than neo-arsphenamin until a reversed experiment gave similar results.

SUMMARY

1. The effect of sulpharsphenamin on the Wassermann reaction in a series of sixty-nine patients with acquired and congenital syphilis has been studied by periodic measurements of the Wassermann antibody. The results in these particular cases are reported and observations are made on some of the variable factors influencing the serologic effect of treatment.

2. The negative Wassermann reaction has been used by many investigators as a therapeutic index of the effect of antisyphilitic drugs. Such comparisons will prove untrustworthy unless due allowance is made for (1) the amount of previous treatment, (2) the stage and duration of the disease, (3) the initial strength of the reaction and (4) the length of time after treatment before a minimum reduction is reached. In a series of forty patients with a strongly positive reaction, a negative reaction was obtained in 33 per cent. The patients who had received previous treatment yielded 27 per cent. negative reactions, as compared with 43 per cent. for those who had received no previous treatment. Patients who had had syphilis less than four years gave twice as many negative reactions as those who had had syphilis for more than four years. Patients with reactions above 16 units in strength had only one-third chance to attain a negative that reactions of less than 16 possessed. Except in secondary syphilis, all the negative reactions did not occur until eight or more weeks after treatment.

3. The quantitative Wassermann method by eliminating certain shortcomings of the qualitative test serves as a more useful guide to treatment. Our measurements of the Wassermann antibody not only indicate the production of a simple negative, but demonstrate changes irrespective of the strength of the reaction, and afford a more delicate reading within the negative zone. An average reduction in the Wassermann antibody of 52 per cent. in adults and 56 per cent. in children was obtained after a five weeks' course of treatment with sulpharsphenamin. The maximum effect was not obtained, except in secondary cases, until twenty weeks after treatment had ceased.

4. Among the factors that influence the reduction of the Wassermann antibody are: (1) individual variation, (2) initial strength of the reaction, (3) the duration of the disease, (4) previous treatment and (5) dosage.

Individual variation in serologic response to treatment is particularly noticeable. About one-third of our patients showed no change, one-third showed a moderate change and one-third, a marked reduction of the Wassermann antibody.

The high titer initial reactions, above 8 units, show twice the reduction of those below this strength.

Syphilis of less than four years' duration gives twice the reduction of syphilis of more than four years' duration, the difference being particularly marked in patients who have received no previous treatment. Secondary syphilis gives the most rapid and complete response to treatment, the reaction falling to a minimum four weeks after treatment. Children who show stigmas of congenital syphilis respond less readily than those with latent cases.

Patients who have received previous treatment with arsphenamin show about one-half the reduction of untreated patients, whereas mercury does not produce this resistant condition. A comparison of results of treatment with mercury and sulpharsphenamin in the same children showed that the latter had about twice the efficiency of the former. Previous treatment with arsphenamin either leaves a more resistant fraction of the Wassermann antibody or tends to produce a treatment-fast condition to sulpharsphenamin. Wassermann-fast patients are found in one-sixteenth of untreated as compared with two-fifths of treated patients. Theoretically, it seems that long continued use of an arsenical drug is less satisfactory than short time intensive treatment with several remedies. Sulpharsphenamin, although slightly different than arsphenamin, does not offer a sufficiently radical change to offset this arsenic-fast condition.

The weekly rate, typifying intensity of treatment, proved a greater factor than total dosage in influencing the reduction of the Wassermann antibody. The resistant, previously treated patients seem to respond more readily to intense treatment, whereas the reaction in those with early untreated syphilis shows the same reduction with one-half and the full maximum dose. Thus treatment insufficient for the eradication of the disease may easily produce a negative reaction, and the physician who relies on the Wassermann reaction as a guide to treatment may be lulled into a sense of false security to the subsequent detriment of the patient.

PROTEIN SENSITIZATION IN PRURITUS WITH LICHENIFICATION

PRELIMINARY REPORT *

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INTRODUCTION AND DEFINITION

The term "pruritus with lichenification," first suggested by Brocq, is used to designate a fairly well-defined clinical entity more familiarly known as lichen simplex chronicus, and to which the French name neurodermitis is often applied. The condition is a relatively common one in all large centers of population, and many dermatologists consider it a form of eczema. Brocq, in his voluminous contributions, has shown that the condition differs from eczema both clinically and microscopically, and his views and contentions have been confirmed often by other and more recent investigators, such as A. Alexander, Bukovsky and Highman.

Clinically, the condition occurs either as a primary or a secondary eruption. In the primary form, large or small areas of apparently normal skin become more or less intensely pruritic; the patient scratches and rubs these areas until the skin becomes inflamed and later thickened; after a while the affected areas assume a glazed appearance, and the surface presents the characteristic cross-hatching and formation of pseudopapules, making up the picture of lichenification. This primary variety is more common in children. In the secondary form, the lichenification is engrafted on, occurs coincidentally or sometimes succeeds an existing pruritic eruption, such as scabies, eczema, pediculosis, mycosis fungoides, etc. The clinical and histologic changes in both varieties are practically identical.

ETIOLOGY

As to its etiology, various views are held by different observers. Brocq, in his early publications, maintained the view that the disease occurs in neurotic persons, and that excessive indulgence in condiments, tea, coffee, alcohol and tobacco is a prominent contributing factor in the causation of the eruption. Bukovsky believed that a blood-borne toxic

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* Read at the Forty-Seventh Annual Meeting of the American Dermatological Association, held at Minneapolis, June, 1924.

agent, acting on the peripheral nerve terminals even before macroscopic changes occur in the skin, provoked the itching and caused the vascular dilatation and the edema which were disclosed by the microscope. Ehrmann, after investigating a large group of cases, concluded that the condition was directly related to functional disturbances of the gastro-intestinal tract and that malfunction, especially of the pancreas, played an important part in its causation; he differentiates two groups: one embraces gastro-intestinal disturbances of motor and secretory nature and is divided into several subgroups, such as anacidity, hyperacidity, disturbances of pancreatic digestion, gastric atony, etc.; the second group points to a direct relation to abnormalities of the internal secretions. He calls attention to the frequent association of cutaneous lichenification with urticaria, dermographism and malfunction of the thyroid gland. Spiethoff made analyses of the gastric juice in a number of patients, and found marked deviations from the normal in the hydrochloric acid content, but he does not attribute the eruption itself to disorders of gastric function.

Ehrmann read a paper on neurodermitis at the thirteenth congress of the German Dermatological Society, held at Munich in May, 1923. In this paper, he emphasized the rôle played by anaphylaxis in the causation of the eruption, and the fact that a certain proportion of the patients also had asthma.

It was the occurrence of asthma and hay-fever in some of our own patients with neurodermitis that lead us to an investigation of the protein sensitization phenomena exhibited by this class of cases.

In a group of cases of neurodermitis tested, definitely positive skin reactions to various proteins were obtained by the skin scarification method. In some of these cases, definite improvement resulted from the elimination of the protein, giving a positive skin reaction, and in one case reacting to pollens, improvement followed active immunization with the specific pollen.

In testing these cases, it is important to make a complete test, using the various foods, pollens and epidermals. Patients should be tested, preferably between attacks if possible, for if tested during the height of an attack, they will often fail to give a skin reaction to proteins to which they are actually sensitive.

In the treatment of patients giving a positive reaction to various proteins, it is advisable to eliminate completely the protein giving a positive reaction in the case of the foods, with the possible exception of wheat, milk and eggs, when active immunization should be attempted. Though quite successful, active immunization with pollens and epidermals is not permanent and must be repeated.

A brief outline is given of a few of the cases tested which gave positive reactions; these are presented merely as picked examples, as a great many patients tested do not react to any protein. However, we feel that all cases of neurodermitis should be tested completely, as a sufficient number are truly allergic in origin, and this is the only way of properly classifying and grouping them.

REPORT OF CASES

CASE 1.—J. S., a girl, aged 3, had neurodermitis of the neck. There was a positive reaction to salmon and spinach. This patient improved rapidly on roentgen-ray treatment, and the eruption did not recur after elimination of salmon and spinach, both of which this patient had been taking regularly.

CASE 2.—S. M., a boy, aged 11, had neurodermitis of the arms and neck. There was a positive reaction to carrots, rice and tomatoes. The eruption cleared up completely on removal of rice, tomatoes and carrots from the diet. The patient was tested in July, 1922, and had had no recurrence. No other treatment was instituted.

CASE 3.—C. M., a woman, aged 35, had neurodermitis on the neck, arms and face. A similar eruption appeared nearly every year during May and June. The duration of the illness was twelve years. A strong skin reaction to timothy, red top and sweet vernal grass was obtained. Injections of these pollens were given, and the eruption quickly disappeared; the patient was free from eruption during the remainder of the season for the first time in twelve years.

CASE 4.—H. O., a man, aged 50, had neurodermitis of the arms and neck. There was a positive skin test to egg yolk, beets, cabbage and strawberries. No improvement followed the removal of these foods from the diet.

CASE 5.—W. O., a man, aged 31, had neurodermitis on both sides of the face for eight months. There was a positive reaction to coffee, corn, grapefruit and salmon. Definite improvement followed the removal of these proteins from the diet.

CASE 6.—M. R., a girl, aged 3, had had neurodermitis of the wrist and knees for the past year. She had had persistent bronchitis during this time. There was a slight reaction to beets, celery, egg yolk, apples and peaches, and a strong reaction to egg albumin. The eruption improved markedly, particularly on the removal of egg white, and the bronchitis materially improved.

CASE 7.—M. W., a woman, aged 35, had neurodermitis of both arms. There was a positive reaction to goose feathers and cat's hair, also to tea and coffee. This patient was advised to sleep on an air pillow, eliminate tea and coffee from the diet and was given injections of cat hair. The eruption improved materially on this treatment.

CASE 8.—L. H., a woman, aged 20, had had neurodermitis on the neck for the past six years. A strongly positive reaction was obtained to lactalbumin and whole milk. This patient was tested recently, and therefore we could not conclude as to the results of treatment.

CASE 9.—J. H., a man, aged 42, had neurodermitis of the arms and legs. A strongly positive reaction was obtained to sulphur, and a slight reaction to goose feathers and clams. This patient worked in a hat factory where

he was constantly exposed to sulphur. He was advised to avoid exposure to sulphur, but as tests were performed recently, we cannot comment on the results of the treatment.

Case 10.—R. K., had neurodermitis of both arms and hay-fever of both spring and autumnal type. The duration of both the hay-fever and neurodermitis was from three to four years, and there seemed to be a clinical relationship between both conditions. A positive skin reaction was obtained to beans, celery, corn, potato, rye and wheat, also to timothy, orchard grass and ragweed. This patient was tested recently. It is too soon to come to any conclusions regarding the results of treatment.

COMMENT

In commenting on the foregoing briefly outlined cases, we wish to emphasize again the fact that a great many patients with neurodermitis do not react to proteins, but a sufficient number do react and are benefited by the removal of the offending protein to justify testing in all suspected cases and to justify the further study of this condition from an allergic standpoint. In a few other cases that have not been enumerated, there was a definite relationship between the neurodermitis and either persistent bronchitis or definite asthma, which, together with the neurodermitis, were materially benefited by the removal of proteins giving a positive skin reaction. From our series of positive cases, it is interesting to note that we have obtained reactions in cases of neurodermitis not only to the foods but also to pollens and animal emanations. It may be possible to divide the cases of neurodermitis in a similar way to our present classification of bronchial asthma, namely, into the allergic and nonallergic types.

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DISCUSSION

Dr. Jay Frank Schamberg, Philadelphia: I believe the whole subject of cutaneous tests with relation to allergic reactions in the skin is in a somewhat confused state. This may be due in part to the technic. Some years ago we made our antigens, and in our own laboratory determined the amount of nitrogen in each antigen, which should be done in all cases. We had a much larger percentage of reactions with the intradermal injection of the fluid antigen than with the scarification method with the dry antigens on the market. During the past year, although I have used a large number of cutaneous scarification tests for eczema, it has been extremely rare for us to obtain a positive reaction.

I was particularly interested in Dr. Wise's remarks concerning reactions from some of the pollens in certain cases. In a woman who had had difficulty for many years, I found all the food tests negative, but obtained a definite reaction to ragweed and dandelion. I had an extract made from these plants, and gave this in ascending doses to the patient in a similar manner to that in which we use *Rhus toxicodendron*. She obtained greater relief from this procedure than she had experienced in many years. She also suffered from asthma but not from hay-fever.

In another patient, who had rosacea and who had suffered from hay-fever for some years, we attempted to secure desensitization with pollen extract by mouth, with the result that last summer when it was used she had almost complete relief, whereas the injection treatment had not produced relief the previous summer. In my original paper on desensitization against ivy poison, I suggested that this internal method might be tried to desensitize patients suffering from hay-fever, as the internal medicine could be used more continuously and one could make the dosage as large as desired.

The whole subject is full of interest. I think no one is in a position today to evaluate the skin tests with respect to their worth in cutaneous diseases. This presentation by Dr. Wise will stimulate us to make these tests in cases of neurodermitis.

DR. TOWLE: Did you use the whole plant—the flower, stalk and all?

DR. SCHAMBERG: The work was done by a pharmacist and I do not know just how he made the extract, but he is a man of high standing in his profession.

DR. ERNEST DWIGHT CHIPMAN, San Francisco: I should like to know whether there were any cases of neurodermitis in which the patients were sensitized to proteins of bacterial origin.

DR. WALTER J. HIGHMAN, New York: I think the point about neurodermitis is that it is a definite syndrome and must have a definite causation. I think the widest scope will be furnished by the view Dr. Wise indicated. I think Drs. Wise and Ramirez have furnished us a significant piece of work in indicating that a substantial majority of the cases are due to sensitization. The disease occurs at definite locations; it starts with itching, and sooner or later lichenification appears. The condition occurs in the neurotic type of patient, whatever that may mean, but there is no question that the sympathetic nervous system, the vasomotor system and so on play an important rôle, and I think this together with Dr. Wise's findings will give us a distinctly better concept of the subject.

DR. FRED WISE: As Dr. Schamberg has pointed out, the subject is complex. Neurodermitis is subject to many vagaries, and I do not find fault with any one for calling these conditions eczema in many instances; but those who have paid much attention to the condition, as I have in the last few years, know that there is a true neurodermitis. One of the interesting features is that an investigator of the acumen of Ehrmann, who says he has studied the disease for thirty years, believes it is due to gastro-intestinal disturbances. That brings up the subject mentioned by Dr. Highman, the polyvalent type of case; but the striking frequency with which we encounter patients with neurodermitis who give a history of asthma, bronchitis or hay-fever, both in the clinic and in private practice, in a percentage that does not occur in eczema is remarkable.

In answer to Dr. Chipman's question, we have not come across a case in which we have definitely proved bacterial infection, but this work is merely preliminary, and we hope to present a more comprehensive report later

MONILIA AS A POSSIBLE ETIOLOGIC FACTOR IN PSORIASIS*

PRELIMINARY REPORT

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AND
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Repeated and constant effort to determine the factor or factors underlying the cause of psoriasis has led to no definite knowledge. Whether this disease is due to a living agent, to nutritional unbalance or to a lack or an excess of certain substances within the affected organism is a moot question, and there may be found supporters of all and any theories concerning the etiology of psoriasis.

We wish to present briefly the results of a study of a number of cases of psoriasis. The fact that fungi imperfecti are the causative agents of a number of dermatologic lesions, as well as our own observations that organisms similar or identical with those found in the lesions were also present in the feces in some such cases, led us to search for organisms of this type in cases of psoriasis.

We have made cultures from the scales, the blood and feces in cases of psoriasis. The medium used was a Sabouraud's medium, made with American products (peptone, Difco, and maltose, C. P.). In all, thirty cases have been studied, but we did not obtain all three types of specimens from each case.

We have found in the feces from nineteen of twenty-three cases, *Monilia* or monilia-like organisms. In the blood from four of twenty-four cases, similar organisms, identical with the ones isolated from the stool, were found. In an additional case, organisms were seen in smears from the blood cultures, but we were not able to cultivate or isolate them. From the skin scrapings (scrapings from the deeper portions of the lesions are preferable), the organisms were demonstrated in eleven of twenty-four cases, being cultivated in seven cases and only demonstrated in the cultures in four cases.

We have examined the feces from normal persons and have found, in approximately 100 cases, *Monilia* present in 6 per cent. In blood cultures from normal persons, we have, in a small series, never found *Monilia*, and in skin scrapings from the extensor surfaces of the arm,

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about the elbow, we were unable to cultivate *Monilia* in any of our twenty-seven cases.

The finding of *Monilia* in the stool in such a large percentage of cases of psoriasis, and the finding of organisms identical to those demonstrated in the feces in a fair number of cases, in the blood, and particularly in the scales, suggests strongly that we are dealing, in *Monilia*, with organisms bearing some causal relation to this disease.

That *Monilia* is not normally present in the blood and on the skin of unexposed portions of the body, and that they occur in the feces in only a relatively small percentage of normal persons is evident from our series of observations.

A limited number of patients with psoriasis have now been treated with vaccines prepared from these monilia organisms—usually an autogenous vaccine. Thirteen patients have been treated; in a considerable number there has been improvement, and in some an almost complete clearing of the condition; however, sufficient time has not elapsed to state whether the clearing of the condition was anything more than a chance temporary improvement, such as is frequently noted in cases of psoriasis. However, one case is possibly of interest—a case of over twenty years' standing, in which, following vaccine treatment, the condition has now cleared up more than it has at any previous time. It appears at least that the use of the monilia vaccine is of some value in treatment of psoriasis.

It should be stated that while all the organisms isolated from the cases of psoriasis are *Monilia* or closely related to *Monilia*, they are not all identical. We have, of course, an analogy to this in a number of other dermatologic conditions, in which several different species, or even different genera, may be the causative agent of a particular clinical entity.

It is possible that in psoriasis it is not one factor alone that plays the etiologic rôle. It may well be that constitutional factors, processes of sensitization to a particular agent, as well as the invasion by a specific organism must be combined in a person, in order that the lesions may appear. If the monilia organisms are of importance in the causation of psoriasis, as we believe them to be, then the fact that they are so constantly found in the feces in such cases suggests the possibility of an enteral sensitization.

In a later communication, we shall present more fully the study of the organisms which we have isolated, as well as additional data on experimental work with these organisms. Suffice it to state that, up to the present, we have not been able to reproduce the disease in either animals or human beings.

SUMMARY

In a series of thirty cases of psoriasis, we have found *Monilia* or monilia-like organisms in the feces in 82 per cent., in the blood in twenty-one per cent., in the skin scrapings in 46 per cent.

In normal subjects, *Monilia* was found in only 6 per cent. of about 100 stools; on the skin of unexposed portions of the body (27 cases) and in blood cultures in no cases.

It appears that the use of a vaccine prepared with these organisms is of some value in the treatment of psoriasis.

These findings suggest strongly that the monilia and similar organisms bear some causal relation to psoriasis.

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THE CLINICAL SIGNIFICANCE OF SOME COMMON DERMATOSES

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For many years, the relation of certain groups of dermatoses to the general condition of the patient has been well recognized by all dermatologists. The entire erythema group, lupus erythematosus and the papulonecrotic tuberculids may be mentioned as examples of diseases in which a search for internal factors and a careful survey of the patient as a whole are necessary to do justice to the patient.

The relation of the commoner forms of dermatitis to the patient as a whole are not so clearly recognized. With the differences between the Austrian and the French school over the relative importance of internal and external causation, this paper is not concerned. Both factors undoubtedly play a part, and their importance varies in individual cases. What we are chiefly interested in is the factor of the patient as a whole in predisposing to any type of local or general irritation or infection, and more particularly the significance of various types of dermatoses as an indicator of more serious troubles in the system elsewhere than on the skin.

SENSITIZATION AND ALLERGY

Sensitization and allergy undoubtedly play an important part in the production of various forms of dermatitis. Varying susceptibility to poison ivy, the occasional patient who is sensitive to primrose and many other less common examples may be cited. On the other hand, these terms are sometimes used all too freely, and are often the easier way to explain eruptions that might be otherwise accounted for by a more careful study of the patient.

THE NERVOUS SYSTEM

The relation of the nervous system to the skin is easily demonstrable from the personal experience of any one. We have all experienced itching of the skin when we encounter a patient with pediculosis or scabies. A similar mechanism can easily be imagined as playing a part in the production of some of the commoner dermatoses.

CASE 1.—*Neurodermatitis.*—E. N., a white girl, aged 11 years, was one of eight patients with almost identical cases seen during the past two years. In all, a definite relation to the nervous system was established. On admission,

the patient presented an eruption of six years' duration. It was located on the back of the neck, on the flexor surfaces of the knees and elbows and about the ankles. The skin in the affected areas was thickened, lichenified and excoriated with scratching. There was considerable scaling. The patient had been under the care of several physicians and had had various local treatments. No one seemed to have given her general condition any thought. She was underweight. Her mother reported her nervous and irritable. She was not doing well at school. Dr. Foxwell examined her and found that she was one and one-half years retarded mentally, and was suffering from a definite neurosis. There was no evidence of organic disease, nervous or otherwise. This patient improved considerably under roentgen-ray and soothing local treatment and the proper care of the neurosis, but had a relapse when the care of her mental condition was neglected.

Case 2.—*Seborrheic Dermatitis.*—H., a white man, aged 45, presented a moderately severe seborrheic dermatitis over the face and neck. He had had local treatment, including roentgen-ray, which had first benefited, but later failed to improve, the condition. The eruption caused little discomfort, and bothered him only because of its appearance. There was also a mild element of rosacea in the case. He was advised to use a soothing lotion and was referred to Dr. Perry for gastro-intestinal survey, as his only other complaint was some distress after eating. He was found to be underweight and suffering from excessive intestinal fermentation. He was placed on appropriate treatment and, with the improvement of his general condition, the skin trouble practically disappeared. On returning to his work, however, that of an executive in a large business, he gradually became worse under the strain of close attention to business. The next summer he returned, with a relapse of both skin and abdominal complaints. Under rest and forced feeding at a sanatorium, with proper treatment for the intestinal disturbance, the patient again improved remarkably with only soothing local treatment. We have grouped this case under nervous system diseases because Drs. Clark and Perry concurred in the opinion that the underlying cause of the intestinal trouble, the loss of weight and the dermatitis was the marked nervous tension under which this man had worked for years without proper rest or relaxation. Furthermore, it was the opinion of all that these were warning signs of more serious trouble if he did not alter his manner of living.

Case 3.—Mrs. K., a white woman, aged 50, complained of an itching on the neck and extremities. There was no evident pathologic condition to account for it. No chronic urticaria, senile changes nor evidence of external irritation was found. The condition had started after a series of mental shocks. The patient's mental condition was obviously excited, and she said the itching was worse when she was most "nervous." The patient was seen but once, but phoned later that, following a rest away from home, the itching had stopped.

Case 4.—*Pruritus ani.*—N. H. K., a white man, aged 36, had been suffering for two years from severe itching about the anus and perineum. He had been operated on for fissures that had developed after the itching started, but without relief. He had been married a number of years. Three years before, his wife had had a baby, and since that time he had had increasing difficulty with his wife over sex matters. He was unimproved by roentgen-ray and other local treatment, and injections of streptococcus vaccine. This may have been a case of sex neurosis.

CASE 5.—E. P., a white youth, aged 16, was suffering from a stubborn and severe eczematoid ringworm of the feet, which kept him in bed for weeks at a time, in spite of all usual treatments for this condition. Mycelium was found in abundance at all times during this trouble. He was obviously neurotic, and a diagnosis of dementia praecox was made at a subsequent examination. It is significant that the skin condition has caused him no trouble since he received hospital treatment for his mental condition.

CARDIOVASCULAR-RENAL DISEASES

Diseases of the cardiovascular system seem rarely to be associated with skin diseases in the literature. More careful study in the future, however, may show a relation that now seems infrequent.

CASE 6.—*Pruritus.*—Miss N. B., a white woman, aged 35, was seen in consultation with Dr. King. There was severe decompensation of the heart, with general anasarca. Except for the edema, there was no pathologic condition of the skin. The itching was severe and localized entirely over the edematous areas. Such itching, with edema from cardiac failure, must be unusual, but the clear-cut relation in this case, and the comparative condition in edema of the legs from varicose veins and other conditions, may indicate that careful observation will reveal other cases with a similar relation in which the heart failure is not so marked.

CASE 7.—*Dermatitis.*—S. C., a white man, aged 55, a farmer, appeared at the Georgetown University dispensary complaining of an eruption on the hands and face. The skin in these areas was thickened, red, scaly and on the palms, fissured. The pruritus was marked. The eruption was entirely limited to exposed surfaces. The trouble had been present about five years, and the patient had seen a large number of physicians, who had prescribed various local treatments, without effect. On questioning, it developed that the patient also suffered from intense headaches. He was examined by the medical department, and they reported that the man was suffering from interstitial nephritis, with a marked elevation of blood pressure. Under general treatment for nephritis and a simple local application, the patient was much improved. It seems likely that the retention of nitrogen rendered the skin susceptible to the irritation of the sun, wind and irritants incidental to his occupation.

CASE 8.—Mr. A. P., a Filipino, aged 25, had a chronic, indurated, scaly, fissured and markedly pruritic dermatitis of the hands and face. He had had all kinds of local treatments, including roentgen-ray and ultraviolet light, without much effect. General examination revealed a chronic interstitial nephritis, and he improved considerably in the hospital, under a limited diet, with local treatment. This case is almost similar to the previous one.

METABOLIC DISTURBANCES

The relation of metabolic disturbances to diseases of the skin has received considerable attention recently. Various disturbances in blood chemistry have been shown to predispose to certain types of dermatoses, and continued study will no doubt show other similar relations.

CASE 9.—*Dermatosis Industrialis.*—T. A. M., a white man, aged 30, a printer, eleven years ago, while working at his occupation, developed a dermatitis due to ink. This was promptly relieved when he stopped work. Each time he returned to work the dermatitis recurred. About three years ago, he gave up his occupation and was transferred to another department. In spite of this the eruption recurred. Local treatment with the roentgen ray cleared the eruption several times. In January of this year, the patient again appeared with a recurrence. At this time there was a red, scaly, pruritic dermatitis of the face and neck, upper part of the trunk and legs, with occasional groups of vesicles. An artificial wheal gave a positive reaction. A general physical examination and urinalysis were negative. There was no history or evidence of intestinal trouble. The blood chemistry was normal, except that there were 575 mg. chlorids (normal, from 450 to 500 mg.). The omission of salt from the diet caused a prompt remission of the dermatitis, except in a few localized patches. It seems likely that the excess of salt predisposed to local irritation. The patient has not resumed his trade, however.

CASE 10.—*Neurodermatitis.*—Miss H. M., a white woman, aged 18, had begun to have skin trouble following an attack of whooping cough, at the age of 2, and had suffered almost constantly ever since. She had seen a number of physicians, had had roentgen-ray, ultraviolet ray and various local treatments. She had also taken much medicine by mouth. When first seen, she had erythematous, scaly, excoriated, and markedly lichenified dermatitis of the face, neck and flexors of the arms. Her weight was 87 pounds (39.5 kg.). She was several years behind her age at school. A physical examination was negative. The basal metabolic rate was 8 per cent. Urinalysis was entirely negative on several occasions. Blood chemistry revealed: total nonprotein nitrogen, 60 mg. per hundred cubic centimeters, (normal from 25 to 35 mg.); uric acid, 3.2 mg.; (normal from 1 to 3 mg.); urea nitrogen, 9.2 mg.; (normal from 12 to 30 mg.); creatinin, 152 mg.; (normal from 80 to 120 mg.), and chlorids, 693 mg.; (normal from 450 to 500 mg.).

Under proper dietetic management and soothing local treatment, this patient became much better, but dropped from sight before she was entirely well.

CASE 11.—E. B., a white man, aged 60, had been suffering from pruritus ani for about twenty years. Three years ago he began to notice increased nervousness and some swelling in the neck. This was diagnosed as hyperthyroidism. The basal metabolic rate was + 120. In addition, he later developed prostatic enlargement, which required operation. The pruritus was controlled locally by roentgen-ray treatment, but persistently recurred. The pruritus showed little improvement with the cure of the thyroid and prostatic diseases.

CASE 12.—*Neurodermatitis.*—Miss M. S., a white woman, aged 30, had been troubled for three years with a recurring dermatitis on the back of the neck and flexors of the arms. The patient noted that the eruption was always worse when she was worried over losing her job. There was scaling of the whole scalp, with marked lichenified dermatitis on the back of the neck and flexors of the arms. The patient was large framed, with a dry skin and scanty hair. During the attacks, the hair on the outer eyebrow always fell out. There was also less hair on the scalp. The basal metabolic rate was — 13. Under thyroid medication, her general condition was greatly improved, and her skin was not so dry, but it is too soon to say whether or not the eruption will return.

The relation of gastro-intestinal diseases to various dermatoses is commonly recognized in all textbooks.

COMMENT

Certain objections to any definite conclusions from such a study are recognized: (1) While the cases presented are not all that have occurred in my experience of a similar nature, the total number of cases in which definite relation to constitutional disturbances has been established is not large. (2) Some of these cases are based on clinical inference rather than on clinical fact. (3) The relation of the dermatosis to the constitutional disturbance may be incidental rather than related clinically. Granting all these points, the fact remains that a majority of such patients will be greatly benefited by the discovery of physical defects other than those of their immediate complaint, and no specialty should be so narrow that the patient as a whole is ignored in the study of one system.

I do not underestimate the importance of local and external factors. No improvement can be hoped for if these are not discovered and eliminated when possible.

CONCLUSION

1. Twelve cases of common dermatoses falling in three general groups of constitutional disturbances are cited.

2. Most of these patients have been benefited both in their general health and with respect to their dermatosis by the discovery of constitutional defects.

3. In all chronic or recurrent dermatoses, a general survery of the patient should be made in an effort to establish some underlying cause other than allergy.

THE ROENTGEN-RAY TREATMENT OF VARIOUS DERMATOSES

INCLUDING A COMPARATIVE STUDY OF THE TREATMENT OF ECZEMA OF THE HANDS USING ONE-FOURTH AND ONE-HALF SKIN UNITS *

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With the perfection of the accuracy of dosage of the roentgen ray in the treatment of diseases of the skin, there has been added to the therapeutic armamentarium of the dermatologist the most valuable agent in the history of this specialty. A large number of dermatoses that in former years stubbornly resisted all methods of treatment now lend themselves quite readily to properly applied doses of roentgen rays. We have endeavored to review the results obtained in the past two years in the department of dermatology, and the findings have been pleasing indeed. A large number of diseases are not included in this review, because patients did not present themselves with the necessary frequency and regularity to allow us to draw any positive conclusions. Records with only two or three treatments and no end-result were discarded. It is difficult to interpret the disappearance from observation of dispensary patients with only an incomplete course of treatment. To assume that they were cured would be flattering to our statistics, but, we fear, rather misleading; therefore we preferred to omit this group of cases.

The indirect method of computing dosage was used. We employed the mathematical equation spark gap multiplied by time, multiplied by the amperage, divided by the square of the distance. This is the method advocated and employed by MacKee and his co-workers so successfully over a prolonged period. It is simple of application and has stood the test of time. Our dosage varied according to the disease, but the first dose in all conditions, excepting when destruction or depilation was desired, was always one-fourth skin unit to test the tolerance of the skin, and then subsequent doses varied between one-fourth skin unit weekly and one-half skin unit every two weeks. It is with a certain amount of pride that we add that during the time allotted to the review of this work we have had no bad roentgen-ray effects. This we attribute to the accuracy of our apparatus and to the practice of prescribing a boric acid ointment for one week in all patients before undertaking treatment.

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In the treatment of acne vulgaris, we were able to collect thirty-six cases in which there had been sufficient treatment. Of these, twenty patients were cured, and the remaining sixteen were markedly improved. There were seven relapses, and those occurred usually in from four to six months after completion of treatment, and were subsequently cleared up by a few additional treatments. The dose given was one-fourth unit in nine cases and one-half unit in twenty-seven cases. The average number of treatments was fourteen. Verrucae respond well to the roentgen rays. In a group of thirty patients with this ailment, twenty-six were cured clinically, one patient improved and in three we failed. Our failures were limited to the plantar warts, and our experience does not coincide with the results obtained by H. Fox.[1] This is undoubtedly the best method of treating warts other than the plantar variety. It is painless, and, while not as rapid as electrolysis, there is no scarring. The dosage employed was two thirds of a unit every two weeks, and it required an average of three treatments. The tendency of warts to disappear spontaneously after involution had been started was observed in patients treated by the rays. One girl had ten warts, three on one hand, four on the other and three on her foot. The warts on one hand only were treated, and when they began to disappear the others followed. She was entirely well after three treatments to one hand.

In tinea tonsurans, our results were perfect. Fifty patients were treated using the Kienböck-Adamson method. The entire scalp was treated at one sitting, giving each of the five areas a skin unit without screening, except the face, ears and neck. Depilation took place in from two to three weeks, and hair return varied from three to six months. We had 100 per cent. cures, with no complications. A few patients were treated by depilating only the diseased areas, but we soon discontinued this procedure, because, while waiting for depilation to take place in the affected area, frequently new areas of disease would appear, necessitating complete depilation eventually.

In four cases of dermatitis papillaris capillitii, two patients were given one-half units, one one-third unit and one a whole unit. The average number of treatments was six, all of the patients being improved but none entirely cured. Ten patients with sycosis vulgaris were given roentgenotherapy; one-third unit weekly for three weeks was given to produce depilation, followed by one-fourth unit weekly. Seven were cured and three were improved. An average of nine treatments was given. In the treatment of superficial epithelioma of the basal cell type, the results were satisfactory. Seventy-five per cent. of the patients treated were cured, the remaining 25 per cent. being unimproved and

1. Fox, Howard: The Roentgen Ray in the Treatment of Skin Diseases, Arch. Dermat. and Syph. **9**:13 (Jan.) 1924.

finally treated with radium. It was frequently noted that the cases that failed to respond to the roentgen ray would respond to from 10 to 50 mg. hours of radium. Pruritus ani and vulvae were found to be favorably influenced by the roentgen rays. Usually after the first, and certainly after the second treatment, the itching was considerably lessened, and a resistant, annoying condition converted, giving relief and comfort. About six treatments were required to remove all itching, using one-fourth unit weekly. True keloid failed to respond to the roentgen rays in six cases. The patients were given one unit, followed by two units one month later, but in only one case was there improvement, and none was cured. A number of patients with other diseases, among which were tinea cruris, xanthoma tuberosum, lupus vulgaris, lupus erythematosus, chronic itching and papular eruption of Fordyce and Fox, were treated, with striking improvement.

One patient with ringworm of the nails was cured after twelve treatments of one-half skin units; and in paronychia, the roentgen ray holds forth a most gratifying method of treating a formerly resistant disease. Ten patients have been treated, one with a case of congenital origin, using one-half unit every two weeks, and while all courses have not been completed, the indications are that this will be the treatment par excellence for this condition. The results obtained in the treatment of psoriasis were rather disappointing. While it is true that one obtains improvement and frequently disappearance of lesions under treatment, it is not unusual to have them recur before the treatment has been completed. In lichen planus, both of the ordinary type and the hypertrophic variety, cures are frequently obtained. Nine patients were treated, using a dosage of one-half unit, and seven were cured.

Eczema responds brilliantly to roentgenotherapy. The chronic lichenoid eczema found so frequently on the neck, which has always been a thorn in the side of dermatologists, melts away before the roentgen rays. Sixteen patients with this disease were treated, using a dosage of one-half unit every two weeks, an average of six treatments being used. All were cured; one suffered a relapse four months after apparent cure, and the condition cleared up permanently after two more treatments. A special study was made of the treatment of eczema of the hands, using two series of cases. In one, the dose employed was one-fourth unit weekly and in the other, one-half unit every two weeks. It was endeavored to obtain a comparison of these two methods. In the one-fourth unit series, fifty patients were treated and an average of five treatments were given each patient. Thirty-two, or 64 per cent., were cured; the remaining 36 per cent. were considerably improved, and, of the total number, 15 per cent. had a relapse in a period of from four to six months after apparent cures were obtained. In the one-half unit

series, fifty patients were treated, using an average of five treatments. Thirty-six, or 72 per cent., were cured; the remaining 28 per cent. improved and 5 per cent. had a relapse. The conclusions gained from this study were: 1. By the one-half unit method a slightly greater percentage of cures are obtained. 2. The percentage of relapses is less by the one-half unit method 1:3. 3. It requires twice as long to obtain these results by the one-half unit method.

It was therefore felt that, for dispensary work where the operator's time is a factor, the one-half unit method was preferable, while in private practice, the one-fourth unit method would be the choice, as it allowed more frequent contact with the patient. The results obtained by both methods were satisfactory.

Northeast Corner Twelfth and Rockland Streets.

THE VALUE OF FLUMERIN IN THE TREATMENT OF SYPHILIS*

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A clinical study of the therapeutic value of a new drug is always beset with many difficulties. This is particularly true when one is dealing with a chronic infectious disease, the course of which is characterized by spontaneous remission and relapse. The literature of the last decade pertaining to the chemotherapy of syphilis reveals striking discrepancies between the opinions of different investigators in regard to the value of each new drug introduced.

Recently, since the work of Brown and Pearce [1] on syphilis in the rabbit, and especially since the utilization of the method of nodal transfer as a criterion for cure, a more exact and standardized technic for establishing the spirocheticidal value and therapeutic index of a drug has been developed. However, experimental syphilis in the rabbit and human syphilis as a potential chronic infection presenting various types of reaction between host and parasite and varying grades of response and tolerance to any given drug, constitute entirely different problems. The entire resistance mechanism in the human being in its relation to latency and relapse is highly complex and little understood as yet. The possession of a high spirocheticidal value by a drug for experimental syphilis does not guarantee a proportionally high curative value in the treatment of human syphilis.

The absolute necessity of a sustained treatment, in which both arsenic and mercury are used, preferably in alternating courses, has been emphasized more and more by those interested in the treatment of syphilis. This is particularly important in the early case in which the aim of therapy is not merely the arrest of the disease, but its cure. Here it should also be considered imperative as a prophylactic measure in the prevention of the precocious type of neurorecurrence. Zimmermann,[2]

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1. Brown, W. H., and Pearce, Louisa: Latent Infections with the Demonstration of Spirochete Pallida in Lymphoid Tissues of the Rabbit, Am. J. Syphilis **5**:1 (Jan.) 1921; A Study of the Relation of Treponema Pallidum to Lymphoid Tissues in Experimental Syphilis, J. Exper. Med. **35**:39 (Jan.) 1922.

2. Zimmermann, Ernest L.: Neurorecurrences Following Treatment with Arsphenamin, Arch. Dermat. & Syph. **5**:723 (June) 1922.

among others, has pointed out that this tragic episode occurs particularly in those patients who fail to receive effective mercurial treatment following the first course of arsphenamin.

Despite the numerous preparations and methods of administration that have been introduced, mercurial therapy has proved more or less unsatisfactory. The method of inunction is probably the best, but one is never certain of the cooperation of the patient or of the dosage absorbed by this method. Besides the practical objection of local pain often experienced at the site of the intramuscular injection, there is always the possibility of a cumulative toxic effect by this route. Any attempt to render the mercurialization of the syphilitic patient more effective seems justified.

Intravenous mercurial medication has been employed here and there with varying success ever since its introduction by Baccelli [3] in 1893. The local corrosive action plus the relatively high toxicity for all the different preparations used has tended to limit the general use of the intravenous method. Probably the cyanid has been received with the greatest favor. It was widely used for a time in France during the war.

Flumerin, the disodium salt of hydroxymercurifluorescein, represents an attempt to develop an organic salt which would combine the three factors of therapeutic value, low toxicity and absence of local irritating qualities. For a complete description of the chemistry and physical properties of the drug, with a study of its toxicity for animals and curative value in rabbit syphilis, reference is made to the original article of White and his co-workers.[4] Flumerin is a dark red powder, freely soluble in distilled water. The 2 per cent. solution is stable and self-sterilizing; it does not precipitate protein of blood serum. The drug contains 32.5 per cent. of metallic mercury.

An average of from ten to fifteen daily doses of 5 mg. per kilogram of body weight to a series of eight rabbits caused complete resolution of the lesions in every case, and consistently negative nodal transfers in all of the animals except one. The maximum single tolerated dose in the rabbit is 30 mg. per kilogram. Repeated doses of 10 mg. per kilogram at intervals of two or three days were well tolerated by animals with no evidence of renal damage. The therapeutic ratio is, therefore, 2:1, an index not equaled by any other mercurial.

Subsequent experimental work on rabbit syphilis, comparing the therapeutic effect of flumerin with that of mercuric cyanid intravenously, and mercuric salicylate and red iodid of mercury intramuscularly, was

3. Baccelli: Gazz. med. di Roma **19**:289, 1893.

4. White, E. C.; Hill, J. H.; Moore, J. E., and Young, H. H.: Flumerin—A New Mercurial for the Intravenous Treatment of Syphilis, J. A. M. A. **79**:877 (Sept. 9) 1922.

reported by Hill and Young.[5] These studies indicate the probable superiority of flumerin over the other preparations. Of the latter, the red iodid alone caused any appreciably accelerated resolution of the lesions, and subsequent nodal transfers were positive in each case. These results lose some significance, because the maximum tolerated dose of flumerin was contrasted with the average therapeutic dose of the three other mercurials.

A comparison of the mercurial content of flumerin with that of the cyanid is of interest, since it offers the probable explanation of the superior therapeutic value of flumerin. Cyanid contains by weight about 80 per cent. of mercury as against 32 per cent. for flumerin. However, the tolerated therapeutic dosage of the former is 0.3 mg. per kilogram of body weight as against 5 mg. per kilogram for the latter. This means that the available therapeutic dose of flumerin contains between six and seven times as much metallic mercury as that of the cyanid.

An extensive clinical study of flumerin in the treatment of ninety-five cases of syphilis has been reported by Moore and Wassermann.[6] The majority of patients received an average dose of 3 mg. per kilogram twice or three times a week. On an average, primary lesions healed in twenty-six days following six treatments; secondary lesions required six doses over a period of seventeen days; tertiary lesions healed following eight treatments in twenty-four days. Flumerin also had a striking effect on the Wassermann reaction. On the whole, the results were not so rapidly obtained as might be expected with the arsphenamins but seemed better than those obtained with other mercurial drugs. However, it should be noted that one recurrence of mucous lesions took place during treatment with flumerin, and four recurrences of tertiary lesions developed during a lapse following flumerin treatment. In regard to toxic symptoms, about one-third developed gingivitis after the eighth or tenth injection; urine examination showed only occasional albuminuria and cylindruria, while phthalein tests revealed no renal impairment. In eight cases, vomiting, bloody diarrhea, or stomatitis was of such severity as to interfere with further administration of the drug.

Snodgrass[7] reports a series of twenty-five cases, eight with secondary and seventeen with tertiary lesions. The dosage ranged from 2 to 5 mg. per kilogram of body weight twice a week until ten injections had been received. The rapid disappearance of the secondary manifesta-

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5. Hill, J. H., and Young, H. H.: Experimental Studies with Mercurials in Experimental Syphilis, J. A. M. A. **80**:1365 (May 12) 1923.

6. Moore, J. E., and Wassermann, H.: The Clinical Results with Flumerin in Syphilis, J. A. M. A. **81**:1840 (Dec. 1) 1923.

7. Snodgrass, W. R.: A New Mercurial for the Intravenous Treatment of Syphilis, Lancet **216**:117 (Jan. 19) 1924.

tions in some of the cases was striking. Two patients had relapses while under treatment, however. The healing of the tertiary lesions, especially the ulcerative, subcutaneous, gummatous type was slower, requiring on an average ten injections. The effect on the Wassermann reaction was not striking. The toxic effects were much more frequent than those reported by Moore and Wassermann. In five cases, or 20 per cent., the complications which ensued were sufficient to compel a change of treatment. In six patients, on the other hand, toleration was complete, indicating the great variation in the person's tolerance for the drug. "Flumerin seems much more potent in its clinical effects than other mercurials," concludes Snodgrass.

The object of this clinical investigation was twofold—to estimate the therapeutic value of the drug in human syphilis and to study the toxicity in the different dosages used. Evaluation of a new drug must necessarily proceed from clinical impression and judgment, since the method of accurate clinical control is not available as in the case of experimental infection in the rabbit. This applies not so much to the actual phenomena observed as to the final interpretation of them and comparison of results with those obtained with other drugs. Although the series of cases presented is relatively small, it is felt that they have been carefully studied. Publication of the work has been delayed until a considerable period of time has elapsed for subsequent observation of the patients, including their reaction to other forms of treatment.

CLINICAL RESULTS

A series of twenty-four patients in the New Haven Hospital or dispensary was given a total of 185 injections of the drug over a period of eighteen months. A freshly prepared 2 per cent. solution was always used. The general plan was to give two doses of 3 mg. per kilogram of body weight twice a week, then a second two doses of 4 mg. per kilogram, and the remaining six of 5 mg. per kilogram, providing no toxic symptoms ensued. In that case, either a smaller dosage was resorted to or flumerin treatment was abandoned, depending on the severity of the toxic effects. The average was about 4 mg. per kilogram, which in the adult ranges between 0.2 and 0.3 gm. of the drug. Dosage of 5 mg. per kilogram was exceeded in only one patient.

Twelve of the patients received flumerin as the first form of antisyphiltic treatment. The therapeutic result was not obscured by the administration of any other drug during the primary period of observation. Eleven of the patients had visible lesions, which made them especially suitable for direct observation of the healing effect of the drug. Photographs and frequent measurements were taken and careful progress records kept. The results are summarized in Table 1. Cases

TABLE 1.—*Cases in Which Flumerin Was Used in the First Instance*

Patient	Case	Age	Stage	Lesions	Duration of Lesion	No. of Doses	Total Dosage, Gm.	Average Dose		Duration of Treatment, Days	Clinical Result	Wassermann		Toxic Effects
								Gm.	Mg. per Kilogram			Before	After	
J. B.	1	22	Secondary	Papulosquamous rash; mucous patches	2 wk.	9 (1 in second course)	2.5	0.28	4.5	34	Striking regression after second treatment; lesions healed after eighth treatment	++++	++++	Abdominal cramps and diarrhea following eighth treatment
J. M.	2	36	Secondary	Mucous patches; Anal condylomas	1 mo. 2½ mo.	8	1.85	0.23	3.5	27	Mouth lesions healed after two treatments; anal condylomas healed after five treatments	++++	++++	None
R. A.	3	13	Secondary	Anal and genital condylomas	2 mo.	4	0.8	0.2	3.5	9	Dark-field examination negative 48 hours after first treatment; rapid regression of lesions	?	++++	Mild gingivitis on fourth day
G. L.	4	16	Secondary	Moist papules under breast; condylomas; mucous patches	2½ mo.	2	0.3	0.15	3.0	2	Dark-field examination negative 48 hours after first treatment; rapid regression of lesions	++++	++++	Mild gingivitis on third day
C. S.	5	56	Tertiary	Ulcerative periosteal gumma, left frontal bone Perforation of hard palate	6 mo. 1 yr.	10	1.95	0.2	3.5	21	Slow healing of forehead; moderate improvement in palate	++++	++++	None
F. A.	6	49	Tertiary	Leg ulcers	15 mo.	10	1.9	0.2	3.5	28	Healed after 10 treatments	++++	++++	Mild gingivitis after fifth treatment
C. C.	7	40	Tertiary	Multiple ulcerative cutaneous gummas	1 mo.	2	0.4	0.2	3.5	9	Practically healed in 15 days	++++	++++	None
E. R.	8	45	Tertiary	Leg ulcer	3 wk.	1	0.2	0.2	3.0	1	Striking improvement in lesion	++++	++++	Stomatitis, diarrhea, hematuria
J. S.	9	23	Tertiary	Papulopustular rash	4 wk.	2	0.3	0.15	2.25	5	Moderate improvement	++++	?	Stomatitis, colic, hematuria
L. DeC.	10	48	Tertiary	Aortitis with aortic regurgitation	Symptoms 2½ yr.	10	2.3	0.23	3.5	37	Symptoms increased under treatment	0	++	None
J. G.	11	14	Congenital	Interstitial keratitis	5 wk.	10	2.35	0.23	4.75	28	Slow improvement	++++	++++	None
E. M.	12	14	Congenital	Interstitial keratitis	2 wk.	3	0.5	0.17	3.25	9	Congestion and infiltration increased	Ae Kahn Test +	Ae. Kahn Test +	Albuminuria, cylindruria

are numbered for convenience of reference, not according to the order in which they were registered for treatment. The use of the drug in patients in the primary stage did not seem justified because of the importance to the future welfare of the patient of an initial intensive arsenical course.

The four patients in the secondary stage showed striking regression of the lesions. Healing became complete in Cases 1 and 2, in which treatment was continued through one course. Case 1 is reported in detail. Cases 3 and 4 were used solely for a study of the spirocheticidal power of the drug by means of dark-field examinations of moist genital and anal condylomas. In Case 3, two injections of 0.2 gm. each were given on successive days. Dark-field examination prior to treatment showed great numbers of actively motile *Spirochaeta pallida*. These decreased in number and motility in examinations at twelve hour intervals, until they could no longer be found forty-eight hours after the first treatment. Repeated examinations on six successive days were consistently negative for *Spirochaeta pallida*. By this time the lesions were healed but had not entirely disappeared. The patient had received four doses of the drug. In Case 4, the method of study and the result were identical. Dark-field examination became negative on the third-day—forty-eight hours after the first of two treatments—and remained consistently so. All the lesions were showing striking resolution and the patient was transferred to arsphenamin therapy, without further flumerin treatment.

Of the six cases with tertiary lesions, four were of the ulcerative gummatous type. Case 5 showed slow healing of gummatous periostitis of the forehead and only moderate improvement of the perforation of the palate. This compared unfavorably with the striking healing of the palatal lesion which took place under subsequent arsphenamin therapy. Case 6 showed a steady healing of a large irregular leg ulcer, which was complete after ten treatments over a month's period of time. This result was especially striking, since the patient did not miss a single day's work as a laborer throughout the treatment. Case 7 was considered remarkable enough to be reported separately. Cases 8 and 9 gave evidence of a striking therapeutic effect, but treatment was interrupted due to toxic symptoms.

In Case 10, a patient with aortitis and aortic regurgitation, who had been treated two years previously with the arsenicals and whose serology had become negative, was given a course of ten treatments. The symptoms of substernal and anginoid type of pain which brought him to the clinic seemed to be aggravated by flumerin. Subsequent arsenical therapy had an even more pronounced effect and was discontinued. Relief was eventually obtained by resection of the left cervical sympa-

TABLE 2.—*Cases in Which Flumerin Was Used in Conjunction With the Arsenicals*

Patient	Case	Age	Previous Treatment	Stage	Lesions	No. of Doses	Total Dosage, Gm.	Average Dosage		Duration of Treatment, Days	Wassermann		Clinical Result	Toxic Effects
								Gm.	Mg. per Kilogram		Before	After		
J. C.	13	24	One course of 8 arsphenamins	Secondary	Maculopapular rash, healed	8	1.85	0.23	2.5	28	++++	0	No clinical relapse	None
G. C.	14	32	One course of 8 arsphenamins	Primary	Chancre, healed	10	2.6	0.26	4.0	35	++ (Kahn test +)	0 (Kahn test 0)	No clinical relapse	None
E. E.	15	18	One course of 6 arsphenamins	Secondary	See special report	6	0.9	0.15	3.0	21	++++	++	Relapse of mucous lesions of tongue under treatment	Albuminuria, hematuria; phthalein, —20 per cent.
C. D.	16	33	See special report	Secondary; relapsed under treatment	Papulosquamous rash; moist genital papules	10	2.8	0.28	3.5	70	++++	++++	Striking; see special report	None
M. B.	17	50	One course of 8 arsphenamins	Tertiary	Glossitis and leukoplakia	9	1.9	0.21	4.0	37	0	0	Continued improvement of tongue	None
R. P	18	36	One course of 8 neoarsphenamins	Tertiary	Perforation of palate	1	0.2	0.2	3.0	1	0	0	.....	Severe ulcerative gingivitis
F. F.	19	42	One course of 3 arsphenamins and 5 neo-arsphenamins	Latent	None	10	2.9	0.29	4.0	37	++++	++++	.....	Gingivitis after seventh treatment
H. L.	20	34	One course of 6 arsphenamins; second course alternating	Latent	None	20 (two courses)	4.7	0.23	4.5	(1) 31 (2) 30	++++	++++	.....	None
A. C.	21	41	One course of 10 arsphenamins	Latent	None	10	3.7	0.37	4.25	49	++++	++++	.....	Gingivitis after eighth treatment
J. B.	22	30	Three courses of arsphenamin with interim inunctions	Latent	None; spinal fluid negative	11	2.45	0.22	4.5	63	++++	++++	.....	Gingivitis after eleventh treatment
A. S.	23	48	Four courses of arsphenamin with mercury and potassium iodid	Central nervous system tertiary	Spinal fluid reversed to negative	9	3.1	0.34	4.5	34	++++	++++	....	None
E. W.	24	24	Three courses of arsphenamin with interim mercury and potassium iodid	Latent	None; spinal fluid negative	10	2.7	0.27	4.5	37	++++	++++	.....	None

thetic nerve and ganglion. Two patients with interstitial keratitis were chosen because of the notorious resistance of this lesion to all antisypilitic drugs. In Case 11, the patient improved slowly over the course of one month until the congestion had disappeared after the tenth treatment. This may have represented a natural regression, as the condition had already been present for five weeks before starting treatment. At least the therapeutic effect was no more striking than might have occurred under other forms of treatment. Treatment was discontinued in Case 12 because of marked increase in ciliary congestion and corneal infiltration following the third treatment. A similar effect was subsequently produced by neo-arsphenamin. However, under intramuscular administration of mercuric salicylate, rapid improvement of the eye took place.

The results in twelve cases in which flumerin was used in conjunction with the arsenicals are shown in Table 2. These data do not constitute the type of evidence which enables one to form a direct evaluation of the drug. However, considerable information was obtained in regard to its adaptability and usefulness as part of a program of continuous antisyphilitic treatment. Also, additional light was thrown on the toxicity factor.

Cases 13 and 14 illustrate the type of early syphilis in which the administration of flumerin in the intervals following the arsphenamin courses seems to offer the greatest promise of usefulness. In both of these cases, all clinical evidences of the disease had already disappeared, but the blood Wassermann reaction still showed complete fixation in Case 13 and partial fixation in Case 14. The subsequent course of flumerin reversed the reaction to negative, and there was no clinical relapse. Case 15 represents the only patient who suffered a recurrence under treatment and is reported in detail. Case 16 illustrates the especial benefit received from flumerin by a patient who had suffered a cutaneous recurrence while receiving arsphenamin. It is also the subject of special report.

In Case 17, the improvement in glossitis and leukoplakia, which had already been initiated by previous arsenical therapy, continued with flumerin. Treatment was interrupted by the development of severe gingivitis in Case 18. The next three cases represent latent syphilis without clinical signs of the disease. Incorporation of flumerin in the program of treatment produced no change in the serology. In Cases 22, 23 and 24, there were still "fixed Wassermanns" following a previous prolonged antisyphilitic treatment. One of these patients, Case 23, had originally suffered from nervous system involvement of the vascular type, but the spinal fluid had been reversed to negative under treatment. Spinal fluid examination of the other two patients offered no explanation

for the persistence of the positive serology in the blood. The subsequent administration of flumerin had no effect on the Wassermann reaction in any of the three cases.

Of the twenty-four cases reported in this series, nineteen have remained under observation throughout the period of study. With the exception of the relapse of the mucous lesion of the tongue, which occurred in Case 15 while the patient was under flumerin treatment, no cutaneous or neurorecurrence of any kind has been observed in any of the nineteen patients during the period of observation. The subsequent clinical course under routine treatment has been uneventful. With the exception of the striking reversal of the blood Wassermann tests already referred to in Case 13, the subsequent serologic course of the patients has been variable and about what one would have expected under any plan of active treatment; that is, gradual reversal of the Wassermann test to negative in the early cases and tendency to fixation in the late cases. In this connection, it is of interest that the subsequent extensive use of sulpharsphenamin in Cases 20, 22 and 23 failed to reverse the Wassermann reaction.

TABLE 3.—*Toxic Effects of Flumerin*

Total number of patients	24 = 100	per cent.
No toxic symptoms	12 = 50	per cent.
Mild gingivitis	6 = 25	per cent.
Transient albuminuria and casts	1 = 4.2	per cent.
Severe reaction, interrupting treatment	5 = 20.8	per cent.

TOXIC EFFECTS

The toxic effects of the drug are summarized in Table 3. One half of the patients had no discomfort. A mild gingivitis developed in one fourth of the patients. It usually occurred following the sixth to eighth injections. One patient, Case 12, showed a transient albuminuria and cylindruria while receiving three treatments, but the phthalein test revealed no renal impairment.

However, in five patients (20.8 per cent.), the reactions were severe enough to contraindicate further administration of the drug. Case 1 is most interesting and is reported in detail. It is highly probable that this patient's tolerance for the drug was diminished by too intensive treatment in the first course. In Case 18 the patient reacted unfavorably to the drug because of the aggravation of a preexisting extensive pyorrhea. Examination of the urine was negative and a phthalein test showed 55 per cent. excretion. Likewise, in fairness to the drug, it should be emphasized that the patient in Case 8 was considered beforehand to be a poor candidate for intensive mercurial therapy because of the presence of hypertension (systolic 165, diastolic 95) and albuminuria. In addi-

tion, the teeth and gums were in an unhealthy condition. A small test dose of 0.2 gm. produced stomatitis, diarrhea and transient hematuria, thus indicating poor tolerance of this type of patient for flumerin.

No explanation was found for the toxic symptoms in Cases 9 and 15. They apparently represent true idiosyncrasy to mercury in this form. Six hours following the first injection of 0.2 gm., or 3 mg. per kilogram of body weight, the patient in Case 9 began to have marked salivation and gingivitis. Examination of the urine two days later was still negative, and he was given a second smaller dose of 0.1 gm. During the next three days, he suffered from a bloody diarrhea and increase in stomatitis and gingivitis. Urine examination five days after the second injection showed albuminuria and the presence of red blood cells and casts. Subsequent development of an intercurrent infection and admission to another hospital prevented further study of the toxic effects in this patient. Case 15 is reported in detail. No explanation is offered as to why the drug should have proved particularly toxic to the kidney in her case. The toxic reaction was certainly not predictable in either of these patients.

Flumerin was not found to be an irritant to the vein wall or to cause thrombosis. Slight extravasations, which occasionally occurred, caused only mild local reaction. Vomiting took place on only two occasions immediately after treatment, probably of psychic origin in both instances. No immediate reactions of the nature of vascular shock, such as may occur with the arsphenamins, were observed.

CASE REPORTS

CASE 1.—J. B., a man, colored, aged 22, weighing 135 pounds (61.2 kg.), who was exposed, July 20, 1923, developed a penile sore on August 30, and a rash appeared on October 16. The patient was first seen and admitted to the New Haven Hospital on November 2. Examination of the skin showed a widespread eruption. On the face, especially on the chin, there were groups of papules, while around the nose and mouth were lesions of the annular type. On the palms and backs of the hands, and to less extent on the trunk, there were scattered papulosquamous lesions. There were no moist genital or anal lesions. Examination of the mouth showed a number of denuded papules on the tongue, hard palate, sublingual region, and buccal mucosa at the angle of the mouth. There was a general glandular enlargement. The blood Wassermann reaction was + + + +. The patient also had a profuse gonorrheal urethritis.

Treatment and Course.—On November 2, flumerin, 0.2 gm., 3 mg. per kilogram of body weight, was given. The urine examination was negative. On November 4, flumerin, 0.3 gm., 4 mg. per kilogram was given. There was no change in the skin lesions. On November 5, flumerin, 0.35 gm., 6 mg. per kilogram, was given. There was slight gingivitis. The skin lesions were regressing. On November 6, flumerin, 0.35 gm., was given. The skin lesions were regressing. The urine was negative. On November 7, no treatment was given. "The lesions in the mouth are rapidly clearing; the ones on the hard palate have practically

disappeared. There is no change in the adenopathy." On November 9, flumerin, 0.3 gm., was given. All mouth lesions had healed. The patient was discharged to the dispensary.

On November 13, flumerin, 0.3 gm., was given; on November 15, 0.3 gm. was given. Stomatitis was much improved. On November 22, no treatment was given. "Skin lesions have disappeared except for residual pigmentation in places." The patient had bloody diarrhea lasting twelve hours after the last treatment. Urine examination was negative. On December 6, flumerin, 0.2 gm., was given. General glandular enlargement had regressed. The blood Wassermann reaction was + + + +. Between December 13 and Feb. 7, 1924, the patient was given eight 0.4 gm. doses of arsphenamin. The blood Wassermann reaction was reversed to negative at end of this course. On February 14, flumerin, 0.2 gm., was given. Urinalysis was negative. The phthalein test was 45 per cent. (one hour). On February 28, no treatment was given. For two or three days following the last treatment, the patient felt drowsy, had a backache and diarrhea, and noticed that the urine was dark red. Examination of the urine was negative except for a trace of albumin. The patient was given a month's rest without medication. Since then he has received fairly regular treatment of alternating courses of arsphenamin and inunctions. There have been no cutaneous recurrences. The blood Wassermann test has remained negative. The spinal fluid has not been examined.

Case 7.—C. C., a man, white, aged 40, weighing 125 pounds (56.7 kg.), gave no history of a primary lesion. Ten years before, he had had a generalized skin rash, which gradually disappeared without fever or itching. The patient was admitted to the dispensary on Dec. 20, 1923. One month previously, a few small "pimples" had appeared on the arms. These had steadily increased in size and had finally broken down, causing the patient considerable pain.

Examination revealed about twenty skin lesions on the arms and forearms. They varied in size from 0.5 to 2 cm.; the majority were elevated about 0.5 cm., with purplish pigmentation and surrounded with considerable induration. Four were ulcerated and had sharply circumscribed borders. The base of each ulcer was covered with a foul, necrotic slough. There was a general glandular enlargement but no other syphilitic lesions. The blood Wassermann test was + + + +.

Treatment and Course.—On December 20, flumerin, 0.2 gm., 3.5 mg. per kilogram of body weight, was administered. On December 29, 0.2 gm. was given. The lesions had already shown marked resolution and healing. The patient failed to return regularly twice a week as directed. Examination again on Jan. 15, 1924, showed all the lesions entirely healed except the ulcerative ones, on which there still remained small scabs. This degree of healing, according to the patient, had been present for the last ten days. This remarkable therapeutic result was obtained in approximately fifteen to eighteen days following only two doses at nine-day intervals. There was no effect on the blood Wassermann reaction. The patient has since received an irregular course of treatment without cutaneous recurrence. The Wassermann test remained positive.

Case 15.—E. E., a girl, white, aged 16, weighing 110 pounds (49.9 kg.), gave no history of a primary sore. She first visited the dispensary on Feb. 16, 1923, complaining of a skin rash. Examination revealed a generalized maculopapular and papulosquamous eruption. Coppery pigmentation was striking. There was a general enlargement of the lymph glands. Examination of the mouth revealed numerous mucous patches on the buccal mucosa, hard palate and tonsils. The tongue was extremely rough and fissured, with many elevated denuded areas

surrounded by a white border. There were no genital lesions or scars. The blood Wassermann test was + + + +. The urinalysis was negative.

The patient received six weekly treatments of arsphenamin. Immediately following the sixth injection, there was a severe reaction of the nature of a vascular shock. It was, therefore, thought best to continue intensive therapy in the form of flumerin. Under the arsenical therapy, the skin rash had disappeared entirely, and the mouth lesions had healed except for the mucous patches on the tongue, which showed definite but not complete regression. The Wassermann test remained + + + +.

Between March 29 and April 19, the patient was given six injections of flumerin, totaling 0.9 gm., averaging 3 mg. per kilogram of body weight. During this treatment, the tongue at first showed continued improvement, but subsequently there was a relapse to the condition similar to that observed on admission. Treatment was discontinued at this point because of the urinary findings. Repeated examinations from April 19 to May 4 showed albuminuria and the presence of red blood cells on microscopic examination. The phthalein test before starting treatment had shown a total excretion of 65 per cent. in two hours. Repetition after the development of the albuminuria and hematuria showed a reduction to 45 per cent. Subsequent urine examinations, on May 8 and later, gave negative findings, and phthalein tests showed a return to normal.

The patient later tolerated neo-arsphenamin well, and under an irregular treatment has shown no further mucous or cutaneous recurrences. The blood Wassermann has become negative.

This case represents the only clinical relapse observed in this work, occurring either during or following flumerin treatment. It is also interesting as showing a specific toxic effect on the kidney and the importance of urine examinations in guarding against this factor, even though it is an unusual occurrence.

CASE 16.—C. D., a man, white, aged 33, weighing 182 pounds (82.6 kg.), developed a penile sore about Sept. 1, 1923, five weeks after exposure. Examination on September 26 showed an ulcerative chancre of the prepuce, from which *Spirochaeta pallida* was demonstrated by dark-field examination. The blood Wassermann test was negative, and there were no signs of generalization of the infection.

Treatment and Course.—From September 26 to November 13, the patient received eight weekly arsphenamin treatments. The lesion had healed on November 6. The blood Wassermann reaction remained negative throughout. From November 13 to December 11, the patient used daily inunctions. The blood Wassermann test was + + + + on his return on December 11. From December 11 to Jan. 15, 1924, a second course of six weekly doses of arsphenamin was given. From January 22 to February 25, six intramuscular injections of mercuric salicylate, 1½ grains (0.09 gm.). On March 4, arsphenamin, 0.4 gm., was administered. The blood Wassermann test was + +.

The patient failed to return until May 6, receiving no antisyphilitic treatment in the interim. Examination on that date showed several moist papular lesions of the skin of the penis and an annular lesion of the scrotum. The blood Wassermann reaction was + + + +. From May 6 to June 3, five weekly arsphenamin treatments were given. The lesions slowly regressed during this period.

June 10: "Examination of the skin shows an unusual recurrent rash which has developed during the past week. On the arms and forearms, especially at the wrists, are numerous copper colored and more brownish-red, confluent papulo-

squamous lesions. They are only slightly elevated, roughly symmetrical in their bilateral arrangement, and show heavy scaling at the periphery. On the shoulder and trunk in back are a few scattered, pigmented, but nonsquamous papules. The rash does not itch. The papules on the penis have also relapsed and become moist again. There are no lesions in the mouth." From June 10 to August 12, ten weekly injections of flumerin, totaling 2.8 gm., averaging 3.5 mg. per kilogram of body weight, were given. On July 1, after three treatments, there had been a striking regression of the skin lesions until only a pigment staining remained at the site of a few of the larger wrist lesions. The moist penile lesions were completely healed on June 24, after two treatments.

There has been no subsequent cutaneous relapse. The blood Wassermann reaction on August 5 was + + + +.

This is the type of arsenic-resistant case in which flumerin seems to offer special promise.

SUMMARY

1. Flumerin was found to cause rapid regression and healing of all types of secondary lesions and somewhat slower but steady resolution and healing of tertiary lesions.

2. A fairly active spirocheticidal value was established for the drug. Repeated dark-field examinations of moist condylomas gave negative results forty-eight hours after the first of two daily injections of the drug.

3. No uniformly striking effect on the Wassermann reaction was obtained either when flumerin was used as the first method of treatment or in conjunction with the arsphenamins.

4. One clinical relapse occurred under treatment.

5. A striking therapeutic result was obtained in one arsenic-resistant case. The patient had had a relapse under previous arsphenamin therapy.

6. Five patients developed toxic symptoms severe enough to contraindicate further administration of the drug.

7. In the average case, the optimum dosage was found to be approximately 4 mg. per kilogram of body weight, preferably twice a week, until a total of from eight to twelve injections has been given.

8. A marked variation in individual tolerance for flumerin was observed. This was not always predictable and necessitated careful study of the patients for toxic symptoms, including routine examination of the urine.

CONCLUSIONS

The requirements for the final acceptance of a new antisyphilitic drug, as suggested by Stokes,[8] seem to have been fairly well fulfilled in

8. Stokes, J. H.: Proper Course for Proponents of New Methods in Treating Syphilis, J. A. M. A. **80**:1474 (May 19) 1923.

the case of flumerin.[9] The points in connection with its chemistry and toxicity have been carefully studied. Its value in the treatment of rabbit syphilis, carefully controlled by the method of nodal transfer as a criterion of cure, has been thoroughly established. Also, its superior curative power, as compared with other mercurials, has been shown for experimental syphilis. So far as its clinical value in the treatment of human syphilis is concerned, there is substantial agreement between the opinions of the three groups of workers who have studied the drug; that is, flumerin is inferior to the arsphenamin group in therapeutic value, but superior to other mercurials in common use. It should be used only in conjunction with the arsenicals or in patients shown to be intolerant or resistant to them. While the toxicity factor is not a grave menace, it must be carefully guarded against in using this drug.

The chief disadvantage of flumerin seems to be that it complicates rather than simplifies a program of antisyphilitic treatment. The great problem today in the cure of syphilis on a large scale is how to keep the syphilitic patient under a prolonged sustained treatment. Incorporation of injections of flumerin twice a week in the interim between arsenical courses calls for such an expenditure of time, energy and money (on the patient's part) that the therapeutic gain must be definitely proved to be commensurate. In early syphilis, in which the importance of an intensive, sustained, combined arsenic and mercurial treatment is so vital to the future welfare of the patient, both for the production of a permanent clinical and serologic cure as well as for the prevention of the tragic neurorecurrence, the superior value of flumerin seems to outweigh the economic consideration.

9. Announcement of the admission of flumerin to "New and Nonofficial Remedies" was made by the Council on Pharmacy and Chemistry of the American Medical Association in the J. A. M. A. **82**:469 (Feb. 9) 1924. It is manufactured by Hynson, Westcott & Dunning, Baltimore.

PEMPHIGUS

EXPERIENCE WITH THE DAVIS TREATMENT *

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The reports made at the 1923 meeting of this Association by R. H. and W. D. Davis in their "Contribution to the Treatment of Pemphigus," were impressive. During the past year an unusual number of patients with pemphigus have been presented, on whom the treatment described by the Drs. Davis has been followed by Dr. Earl D. Osborne, my associte, and myself. This series of cases is reported. The dosage consisted of 0.065 gm. iron cacodylate in ampules and 1.5 c.c. of a 3 per cent. solution of coagulen.

REPORT OF CASES

CASE 1.—*History.*—A woman, aged 39, admitted to the hospital, Aug. 15, 1923, eighteen months previously, February, 1922, had had bullae in the mouth and pharynx. Intermittent attacks therein followed for more than a year, when suddenly bullae appeared all over the body, persistently recurring in crops.

Examination.—The mouth showed red, superficial ulcers on the tongue and on the buccal mucous membrane, while on the body were numerous dime-sized, crusted lesions intermingled with recent bullae. The coagulation time of the blood was three minutes. Otherwise the examination was negative. The condition was diagnosed as pemphigus chronicus.

Treatment.—Two courses of intravenous injections of iron cacodylate and subcutaneous injections of coagulen were administered on alternate days for six weeks with an interval of four weeks. During the interval, two small crops appeared, each of about twelve bullae. The patient was discharged during the holidays, to all appearances well. Since leaving the hospital, she has had no recurrence.

CASE 2.—*History.*—A woman, aged 65, admitted to the hospital, Sept. 26, 1923, said that on April 1, 1923, an eruption had appeared on the hands, quickly spreading over the forearms, then on the legs, rapidly spreading upward and involving the entire body in a week. The eruption was accompanied by itching. This patient has been under observation from the beginning, and at first was given treatment according to the older methods, with the usual remissions and exacerbations which duplicated the first attack.

Examination.—On admission there was elevation of temperature (103 F.) and rapid pulse; denuded surfaces were present in the mouth, throat, larynx, trachea and nose, as well as a few medium-sized bullae, causing a harsh voice and an irritating cough. The cutaneous surface everywhere presented bullae varying in size from that of a pea to that of a hen's egg, usually oval; some were tense,

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some flaccid; some were in flat-forming, circinate figures; some had coalesced; some showed recent formation, and most occurred on an erythematous base. Intermingling with lesions were areas of marked pigmentation causing a negroid appearance, and associated with these were areas of loss of pigmentation. The contents of the lesions were clear, cloudy or opaque, according to age.

Treatment.—Three courses of intravenous injections of iron cacodylate and subcutaneous coagulen on alternate days were administered. The first course was of two months' duration, followed by an interval of fifteen days; the second course lasted one month, followed by an interval of one month; the third course lasted one month. As the treatment progressed, the formation of new lesions became lessened. On May 15, 1924, after no treatment for six weeks, the patient reported having had an occasional development of a small crop of new lesions. The general health was much improved, any complaint being due to other ailments.

CASE 3.—*History.*—A man, aged 18, seen Oct. 1, 1923, said that in August, 1923, he had had a slight pus infection on the fingers and neck following trauma. Three to four days thereafter, the eyes became sore, and blisters appeared on the cheeks. In rapid succession, the arms, hands, legs and trunk became involved.

Examination.—This revealed large and small bullae on an inflamed base distributed over the trunk, extremities, neck and scalp. The larger were from ½ to 1 inch (1.2 to 2.5 cm.) in diameter. Some had ruptured, leaving areas of denuded skin. Lesions were found in the mouth and on the lower lip. The condition was diagnosed as pemphigus chronicus.

Treatment.—Two courses of intravenous injections of iron cacodylate and of subcutaneous injections of coagulen were administered on alternate days. The first course lasted thirty-six days, by which time 90 per cent. of the lesions had cleared up; after an interval of one month, a second course was given over a period of eighteen days. Although the integument became practically clear, it showed numerous erythematous patches and pigmented areas, and it was peppered with whitish-yellow milia. The nodules were so numerous on the soles and palms that in certain areas they had coalesced to form plaque-like elevations. On May 23, 1924, the milia had disappeared, except from the palms and soles. The weight before the onset of the illness was 162 pounds (73.5 kg.); on Oct. 1, 1923, it was 110 pounds (50 kg.). There was a marked appearance of emaciation and toxicity. At the end of the first course the weight was 125 pounds (56.7 kg.). At the end of the rest period, the weight was 135 pounds (61.2 kg.). On May 1, 1924, the weight was 158 pounds (71.7 kg.). There was no recurrence. The general condition was excellent. The patient improved rapidly after the febrile reaction that followed an injection.

CASE 4.—*History.*—A woman, aged 48, seen Nov. 11, 1923, said that in March, 1923, she had noticed "blisters" in the mouth that "came and went" until October, 1923, when blebs appeared on the cutaneous surface, widely distributed but most profuse on the legs. The general health was excellent.

Examination.—This revealed ten lesions in various characteristic stages of development. The condition was diagnosed as pemphigus chronicus.

Treatment.—Courses of intravenous injections of iron cacodylate and subcutaneous injections of coagulen on alternate days were recommended. The patient's physician wrote, under date of May 14, 1924, that treatment was carried on as suggested for a couple of months, during which period the patient developed one or two new areas which, however, rapidly cleared up.

and that in two or three weeks, they were healed. The treatment was then dropped for a month. However, on almost the exact day she was again to begin treatment, she developed a tremendous, acute exacerbation on the leg that was slow to heal. This was about March 1, 1924. Since that time, she had been coming in every other day for treatment. The leg had been healed for two weeks. Recently two areas developed on the face, with no bleb formation and none of the definite symptoms of pemphigus, merely suddenly appearing red areas. There was one on the left cheek about 4 cm. in diameter, slightly indurated. It disappeared in about one week. Whether that had anything to do with her original condition, is problematical.

CASE 5.—*History.*—A woman, aged 21, had a condition that began with bullae and vesicles on the face, soon followed by a large number of blebs in the mouth and on the arms. The lesions gradually became generalized, and the case was diagnosed and treated as ivy poisoning.

Examination.—On Jan. 19, 1924, there were bullae everywhere in great numbers, in the mouth, on the face, on the conjunctiva and on the trunk and extremities. The patient was bedridden, weak and emaciated; she had lost 35 pounds (16 kg.)—from 142 pounds her weight had gone down to 107 pounds (from 64.4 to 48.5 kg.). The condition was diagnosed as pemphigus chronicus.

Treatment.—Two courses of thirty intravenous injections of iron cacodylate and subcutaneous injections of coagulen were administered every other day. During the second month, an injection was followed by a severe febrile reaction. A marked improvement then began. All the bullae had disappeared by the end of the first course; only the vesicles and many erythematous blotches remained. An interval of one month was followed by a second course, since which time no bullae have developed, especially since the erythematous areas had cleared up, leaving the skin, however, studded with whitish-yellow papules like milia. The general health was markedly improved; the weight was 125 pounds (56.7 kg.).

CASE 6.—*History.*—A woman, aged 56, was admitted to the hospital, Feb. 2, 1924, with a condition that began Sept. 10, 1923, with the occurrence of blebs and vesicles between the shoulder blades. The eruption spread gradually over the entire body, including the face and extremities.

Examination.—There was hardly a part of the body not covered by the lesions, which came out in crops; the bullae or vesicles were never of great size, seldom larger than the small finger nail. The lesions ruptured readily, the rapidly drying serum giving the appearance of greasy scales. With the exception of weakness, the patient's general health was good. The condition was diagnosed as pemphigus foliaceus.

Treatment.—Intravenous injections of iron cacodylate and subcutaneous injections of coagulen were given on alternate days. The patient developed lobar pneumonia and died on the sixth day after admission. There was no necropsy.

CASE 7.—*History.*—A man, aged 75, admitted to the hospital, Feb. 6, 1924, had had a sore throat with hoarseness two weeks previously. An eruption on the feet soon followed, which spread gradually over the entire body, including the face, and which was accompanied by intense itching.

Examination.—Examination of the mouth revealed several erosions from ruptured bullae, the largest being on the tonsils. Irregularly scattered over the chest, abdomen, back, face, ears, arms and legs, were bullae and crusted lesions varying in size from one-eighth to three-fourths inch (3 to 19 mm.) in

diameter. There were many excoriations from scratching. The condition was diagnosed as pemphigus chronicus.

Treatment.—Intravenous injections of iron cacodylate and subcutaneous injections of coagulen for about six weeks, on alternating days from Feb. 7 to March 25, 1924, were advised. In two weeks there was marked improvement. During the last four weeks, there were no new lesions. On discharge, the patient was apparently in good health. This patient, an old man, was in a pitiable condition on entrance, but on leaving, after only a few weeks' treatment, appeared to be another person.

CASE 8.—*History.*—A woman, aged 21, whose illness began two months previously, three days after childbirth, was admitted to the hospital on Feb. 19, 1924. She had numerous irritating vesicles and bullae on the lower extremities and on the abdomen, which spread upward over the body and face so that within three weeks the entire body was involved.

Examination.—This revealed many crusted, erythematous lesions, the sites of former bullae, together with recently formed bullae over the entire cutaneous surface. The patient was weak, had lost weight and constantly presented a slight elevation of temperature. The blood picture showed no marked changes. The urine was normal. The condition was diagnosed as pemphigus chronicus.

Treatment.—Intravenous injections of iron cacodylate and subcutaneous injections of coagulen were administered on alternate days for five weeks. The patient was discharged on May 7, without evidence of recently formed lesions, restored to good health.

CASE 9.—*History.*—A man, aged 72, became ill on March 6, 1924, two weeks before the only examination made.

Examination.—The patient was bedridden and weak and complained of intense itching. There were large and small vesicles and bullae widely distributed, together with numerous dried-up lesions. The mouth, ears, face and trunk especially were invaded. The condition was diagnosed as pemphigus chronicus.

Treatment.—Intravenous injections of iron cacodylate and subcutaneous injections of coagulen were given on alternate days. Improvement was marked at first. Albumin appeared in the urine, and treatment was discontinued before the first course was completed.

CASE 10.—*History.*—A woman, aged 66, seen on March 13, 1924, said that in June, 1923, blisters appeared in the mouth. The teeth were extracted without effect on the recurrence of the lesions. The lesions continuously appeared and retrogressed, so interfering with deglutition that nutrition suffered and weakness supervened.

Examination.—The buccal mucous membrane on both sides showed recent lesions and superficial denuded areas on the sites of former bullae. The pharynx also was similarly involved. Later observation showed complete clearing up of the mouth. Similar outbreaks occurred in the vagina. No cutaneous lesions were observed on first examination. On May 3, flat, discrete blebs appeared on the chest and back, occurring daily in crops. They soon dried up, forming bulky crusts. No marked constitutional symptoms were present. The condition was diagnosed as pemphigus chronicus.

Treatment.—Intravenous injections of iron cacodylate and subcutaneous injections of coagulen on alternate days was begun, May 3, 1924. The condition was stationary.

COMMENT

In an attempt to analyze this series, the table was prepared. It shows that there were seven women, ranging in age from 21 to 66, and three men, ranging in age from 18 to 75; that three of the patients were in the period of adolescence, three in middle life and four in old age. It shows five clinical cures and three improvements, all occurring during a period of nine months; while one patient died of an intercurrent disease as treatment was begun, and one has been under treatment for too short a time to expect any change. Eliminating the last two cases, a clinical cure percentage of 62.5 is obtained, with 100 per cent. improvement resulting from the Davis treatment. The clinical cures were obtained from an average of 62½ treatments, covering an average of 10.2 weeks' duration.

It is impossible to make any statement in regard to prognosis from this series, as the time has been altogether too short. It is barely possible that all the favorable results reported herein are merely coincidental with the periods of remission natural in the history of this disease, and that this small series is remarkable only therein. It is also true that these results may be the effect of the injections of a foreign protein.

Nevertheless, in a disease that has so grave a prognosis, especially in the elderly, that causes so much suffering, that is so prolonged and that so increases susceptibility to the onset and fatal termination from intercurrent septic diseases, the prompt and prolonged relief, if not cure, afforded by the Davis treatment easily puts it in the van today for the treatment of pemphigus.

Results in Ten Cases of Pemphigus

Case					Duration of Treatment in	Number of Treatments	Number of Courses	
No.	Sex	Age	Date of Onset	Date Treatment Begun	Days			Results May 20,1924
1	F	39	Feb., 1922	Aug. 15, 1923	112	84	2	Clinical cure
2	F	65	April, 1923	Sept. 26, 1923	154	122	3	One small crop
3	M	18	Aug., 1923	Oct. 1, 1923	84	85	2	Clinical cure
4	F	48	Mar., 1923	Nov. 11, 1923	161	94	2	Improvement marked
5	F	21	Nov., 1923	Jan. 19, 1924	84	60	2	Clinical cure
6	F	56	Sept., 1923	Feb. 2, 1924	3	3	0	Death from pneumonia
7	M	75	Jan., 1924	Feb. 6, 1924	42	47	1	Clinical cure
8	F	21	Dec., 1923	Feb. 19, 1924	35	35	1	Clinical cure
9	M	72	Mar., 1924	Mar. 20, 1924	42	42	0	Improved; stopped because of nephritis
10	F	66	June, 1923	May 3, 1924	20	20	0	Stationary

DISCUSSION

DR. SCHALEK: As long as we have no treatment that is of any value in pemphigus, I think the Davis treatment should be given a trial in every case. I am sorry I did not use it in my case. The remarkable results shown by Dr. Wende seem to be more than a coincidence.

DR. SWEITZER: I have a patient with pemphigus, an old gentleman who has had it for years over the general body surface. When I saw him, he had large

lesions in the mouth, and the cutaneous surfaces were free. This treatment has caused a disappearance of the symptoms. Since hearing the paper of Dr. Davis, and since we have so few cases of pemphigus, I thought I would try it in some other condition. I have used it in two or three cases of dermatitis herpetiformis. I did not cure any patient, but improvement occurred in some. One of the patients died of acute coronary involvement. She had large bullae over the body and hands and marked itching. There was decided relief from this treatment, and the cutaneous eruption disappeared. I thought it might be a good idea to try it in this disease.

DR. WILE: I think these are the most impressive figures I have ever seen on pemphigus, and I should like to know how many of the patients were having their first attack of pemphigus. I have had four serious cases, in which I have attempted to treat the patients with Dr. Davis' method. One I showed to the association last year. This patient was a little girl who had recurrent blebs; she is still under the Davis treatment, without the slightest effect. The other three patients have died. I have frequently noted that patients with pemphigus will occasionally get well from the first attack and then succumb to the second attack. I wondered how many of Dr. Wende's patients had passed through the first attack and were seen during the second.

DR. WENDE: They were all having the first attack.

DR. MORROW: In New York last week I had the good fortune to encounter some cases of pemphigus. I saw three patients, and all had received this type of treatment, one for more than six months and two for more than a year, and there was no improvement in any of them. I think Dr. Fox can tell us about it. I do not understand how Dr. Wende and Dr. Davis obtained their results and why the rest of us cannot get the same effect.

DR. FOX: I have tried the Davis method in a single case of bullous lesions limited to the mouth, in which a probable diagnosis of pemphigus had been made. There was no permanent improvement in this case.

DR. HIGHMAN: I have had three cases myself since I heard Dr. Davis' paper last year. Another case was seen by Dr. Goldenberg, and I know about three other cases. My two patients died promptly. I do not know what became of the one at Mt. Sinai Hospital, for the patient left. I do not know the result in the other two cases, for patients with pemphigus wander a good deal. I have not seen any results comparable to those of Dr. Wende. I cannot reconcile these figures and those of Dr. Davis with my personal observations.

DR. SCHAMBERG: When I heard the paper of Dr. Davis last year I was astonished at the results reported, and I attempted to carry out the treatment in the first three or four cases that came under my care. I could not, however, reconcile the use of these two remedies with my scientific conscience. I thought if a favorable result were brought about, it must be through one or the other therapeutic agent. I have used the coagulen alone in a number of cases. We have had an unusual incidence of pemphigus during the last year, and I have seen no favorable result from coagulen. I had a man, aged 32, with extensive lesions of the mouth and none elsewhere. Coagulen had been administered every other day, with no benefit. This patient died. I have a boy with an extensive bullous eruption, probably a bullous type of dermatitis herpetiformis, which some might regard as pemphigus. He has received this treatment for a considerable period without improvement.

In view of what Dr. Wende reports, I shall endeavor to use these two remedies, but it does not seem plausible to me that the combination of cacodylate

of iron and of coagulen brings about the good result. It appears to me that one of the two substances should be the determining agency; my results with the use of coagulen alone have been nil.

DR. KLAUDER: In a case I saw in consultation soon after returning from the meeting last June, an unmistakable pemphigus, I suggested that a vaccine be made and coagulen administered. The vaccine was administered bi-weekly, alternating with bi-weekly injections of the other agent. During the entire winter, the man was incapacitated, and for some time he was delirious. We thought he was going to die, but he made a gradual recovery, and recently has been up and about. He experiences just a few small lesions now and then, has regained his lost weight and is apparently in good condition. His attending physician told me that when he stopped giving the coagulen, more bullous lesions appeared. The patient's physician religiously carried out the treatment, which is still being continued.

DR. LANE: Of what organisms was the vaccine made?

DR. KLAUDER: A streptococcus was obtained from the bullous lesions.

DR. SCHAMBERG: The only patient among my own series that is living, except in the cases immediately under observation, is a colored woman in whom we carried out the treatment with the vaccine made with an organism derived from her blood—a diplobacillus. There was marked improvement, and the extensive abraded areas and large blebs over her body dried up. She is now in the Philadelphia General Hospital and is in a condition midway between pemphigus and chronic exfoliative dermatitis. At times the skin is dry and desquamating, but the patient is still very weak.

DR. IRVINE: I had one case at the University Hospital last winter. The patient entered the hospital and was put on the treatment recommended by Dr. Davis, but died within a month.

DR. WENDE: I think the most remarkable responses of all in my series were in a man of 75 and in a woman of 66 years. The woman had bullae in her mouth from June, 1923, until March, 1924. She was emaciated, because it was impossible for her to eat on account of the sore mouth. Now the condition of the mouth has cleared up, she is taking food much better, and the lesions have disappeared. I fully appreciate that the time is too short to make any positive claims for the treatment. I am simply reporting the cases, showing the effect that Dr. Obsorne and myself secured in carrying out the treatment suggested by Dr. Davis.

EXPERIMENTAL STUDIES ON IMMUNITY IN HERPES SIMPLEX*

WITH NOTES ON THE INFECTIVITY OF THE BLOOD AND SPINAL FLUID AND ON THE FILTRABILITY OF THE HERPETIC VIRUS

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AND

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It appears definitely established that herpes simplex, irrespective of its clinical variety, is a generalized specific infectious disease with localizing symptoms on the skin (herpetic eruption) and in some instances, particularly herpes progenitalis, in the nervous system. At the present time, this conception of the etiology of simple herpes is based on experimental observations in both the human subject and certain laboratory animals, the rabbit in particular, in whom the active agent, a filtrable virus under certain conditions, produces severe kerato-conjunctivitis and in some instances, varying with the virus or its source, fatal encephalitis.

Although demonstrated many years ago, only recently has it been generally accepted that this disease is both auto-inoculable and heteroinoculable. Teissier, Gastinel and Reilly,[1] after lightly scarifying the forearms of patients presenting simple herpes and others not attacked with simple herpes, inoculated all of them with herpetic exudate. There were thirteen "takes" in sixteen auto-inoculation experiments; the experimental lesions appeared in from two to three days, and their fluid contents were likewise auto-inoculable. There were seven "takes" in ten heteroinoculation experiments. Auto-inoculation "takes" failed to develop after two or three passages, either as the result of the development of an immunity or of a diminished infectivity of the virus. The animal experiments reported in this paper would appear to confirm the latter view. A herpetic exudate that fails to induce an auto-inoculation "take" contains no virus, as experimental controls show. Curiously enough, attempts to inoculate six subjects with material from a herpetic keratitis in rabbits failed. Personal experiments of a similar nature failed in three subjects. However, Schnabel [2] applied some brain emul-

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* Read before the Section on Ophthalmology of the College of Physicians of Philadelphia.

1. Teissier, P.; Gastinel, P., and Reilly, J.: Inoculability of Herpes, Compt. rend. Soc. de biol. **87**:648, 1922.

2. Schnabel, A.: Wien. klin. Wchnschr. **36**:84 (Feb. 1) 1923.

sion from a fatal instance of rabbit encephalitis to his own lip after slight scarification. In from two to three days, typical herpetic vesicles appeared at the site of the inoculation, which disappeared within a week without causing any constitutional disturbances. The contents of those vesicles produced severe keratoconjunctivitis and fatal encephalitis in rabbits. The saliva of Schnabel, before the inoculation had been innocuous to rabbit corneas, but after the herpetic attack it was found to be infectious.

The experimental observations of Teissier and his co-workers have recently been confirmed by Nicolau and Banciu,[3] with special observations on a virus obtained from patients with recurrent herpes. Of twenty-five persons inoculated with fluid obtained from recurrent herpetic vesicles, nineteen "takes" resulted; of twenty-one persons inoculated with fluid obtained from other clinical forms of herpes simplex, fifteen "takes" resulted. In the first group, two of the subjects developed a recurrent herpes at or close to the experimental inoculation.

The transmission of herpes virus to laboratory animals may be accomplished not only with fluid from the herpetic vesicle, but also with spinal fluid,[4] saliva and blood serum [5] obtained from patients during an attack of febrile or corneal herpes. It is not improbable that such is the case with other clinical varieties of herpes simplex.

The mildness of an attack of simple herpes in the human subject is in marked contrast to the frequently severe infection produced in the rabbit. In fact, predisposing factors, and these are extremely varied, seem almost always necessary before the herpetic virus can develop sufficiently in the human subject to cause symptoms, although a rare form, manifestly primary in character, does occur.

As is generally known, herpes simplex developing during an attack of malaria, pneumonia or cerebrospinal meningitis is a diagnostic phenomenon. From an immunologic point of view, however, it is interesting to recall that herpes simplex occurring during the course of such infections occurs only once. Is this indicative of a temporary immunity?

The herpetic virus varies in virulence or infectivity with the herpetic exudate from which it is obtained. Of the three strains used in the experiments herein reported, two produced a mild infection and the third a severe fatal infection in rabbits. The clinical type of herpes simplex does not appear to explain this variation in infectivity. The infectivity of the virus in the human subject in the recurrent types of

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3. Nicolau, S., and Banciu, A.: Compt. rend. Soc. de biol. **90**:138 (Jan. 25) 1924.
4. Ravaut, P., and Rabeau, L.: Compt. rend. Soc. de biol. **88**:1132, 1921.
5. Bastai, P., and Busacca, A.: Klin. Wchnschr. **3**:443 (March 11) 1924.

herpes simplex likewise bears no relation to the age of the infection, as in some it appears to "wear itself out" and in others to increase in frequency, although rarely in severity with age.

There appears to be no natural immunity to herpes simplex in the human subject and, unlike the virus of poliomyelitis, for example, one attack does not ordinarily confer immunity, either general or local. Herpes simplex of the recurrent type frequently occurs in the same area and not uncommonly on the same site as the previous eruption. Such recurrences have been noted as early as fifteen days after the previous attack,[6] and, based on experimental studies in rabbits, the frequency does not appear to depend on the infectivity of the virus.

Although the studies undertaken by us appear to be mainly of academic interest, there is a practical aspect. If an induced immunity could be accomplished in patients with recurrent herpes simplex, a distinct advance would be made in the now uncertain treatment of this frequently distressing and rebellious condition.

EXPERIMENTAL DATA

According to Lowenstein,[7] Luger and Lauda,[8] Doerr and Schnabel,[9] Blanc and Caminopetros[10] and of Levaditi and Nicolau,[11] a rabbit that recovers from a keratoconjunctivitis produced by inoculation with the herpetic virus becomes refractory to future intracerebral or corneal inoculation. This immunity is temporary and lasts about seven months. Levaditi and Nicolau have further shown that a neuro-immunity can be produced by cutaneous inoculation with the resultant establishment of cutaneous resistance. This neuro-immunity after cutaneous inoculation may or may not be associated with corneal immunity. It thus appears that the induction of a refractory state in any section of the ectoderm is followed by the development of a nervous system resistance to the homologous virus. In the production of such areas of local immunity, humoral factors apparently play no part. By direct nervous system injection it is possible to immunize a rabbit so that it will withstand an infective dose of the virus. The immunity is, therefore, associated with tissue or cellular changes only. In animals that have recovered from a herpetic keratoconjunctivitis, no antibodies capable of destroy-

6. Darier, J.: Precis de dermatologie, Paris, Masson and Cie, 1923, p. 171.
7. Lowenstein, L.: München med. Wchnschr. **28**:769 (July) 1919.
8. Luger, A., and Lauda, E.: Wien klin. Wchnschr. **34**:132 (March 24) 1921.
9. Doerr, R., and Schnabel, A.: Schweiz. med. Wchnschr. **51**:469 (May 19) 1921.
10. Blanc, G., and Caminopetros, J.: Compt. rend. Soc. de biol. **84**:629 (July) 1921.
11. Levaditi, C., and Nicolau: Compt. rend. Soc. de biol. **86**:228, 1922.

ing the virus in vitro have been demonstrated. Further evidence that the immunity is only local is the fact that after a rabbit recovers from the infection in one eye, no immunity to infection of the other eye exists, despite the fact that the first eye is refractory. The more severe the herpetic keratitis, the greater (should the animal survive) is the refractoriness to subdural injection.[8] This local immunity disappears in from six to seven months.[12]

Isaicu and Telia,[13] in experimentally testing cross immunity, showed that the virus of simple herpes is identical with the virus of influenzal herpes; corneal vaccination with the one protecting against the other.

Although Levaditi and Nicolau[11] claim that rabbits can be immunized against an active virus introduced in various ways (cornea, skin) and even directly into the brain by progressive dosages, Le Fèvre de Arric[14] was not able to immunize rabbits against herpes by vaccination with fresh virus.

SOURCE AND SUCCESSIVE PASSAGE OF HERPETIC STRAINS

Strain 1 (Table 1).—This was obtained, March 24, 1924, from exudate of recurrent herpes simplex on the forearm of a woman, aged 24. She had had the condition for seven years; it recurred three and four times a year, always at the same site.

TABLE 1.—*Result of Inoculation with Strain 1*

No. of Passages	Material Inoculated	Method of Inoculation	Eye Symptoms	Cerebral Symptoms	Death	Reinoculation
35	Exudate first, later pus from eye to eye	Scarification of cornea	Severe keratoconjunctivitis	Developed average 6 days	Invariable average 10 days	Every third day

This strain was a particularly virulent herpetic virus, producing fatal encephalitis regularly for over thirty passages, but finally mild cerebral symptoms only, without death.

INFECTIVITY OF SPINAL FLUID AND BLOOD OF ANIMALS INFECTED WITH (STRAIN 1)

Experiment 1: Infectivity of Spinal Fluid.—A rabbit, infected in the cornea and conjunctiva five days previously, and showing a marked keratoconjunctivitis with eyelids glued together which, when separated, allowed a thick fibrinous pus to escape, was etherized. Spinal fluid was drawn from the cervical region under aseptic precautions and immediately placed in the conjunctival sac of a normal rabbit, the cornea of which had been scarified. The animal remained

12. Fontana, Arturo: Minerva medica, abst. Ann. de dermat. & Syph., June, 1924, p. 362.

13. Isaicu, L., and Telia, L.: Compt. rend. Soc. de biol. **87**:57, 1922.

14. Le Fèvre de Arric, M.: Compt. rend. Soc. de biol. **90**:978 (April 11) 1924.

normal. From this we concluded that this particular virus did not enter the spinal fluid or, if it did, the amount was so small that no transmission occurred.

Experiment 2: Infectivity of Whole Blood.—A rabbit, inoculated by corneal scarification five days previously and presenting a progressively marked keratoconjunctivitis, severe at the time of bleeding, was bled from the heart in a sterile manner, and the conjunctival sac of a normal rabbit, previously scarified over the cornea, flooded immediately with the blood. No herpetic infection developed. Either there was no virus in the blood, or, if present, it was too dilute (as the concentrated blood experiment below shows), either naturally in the blood or as a result of the traumatic lacrimation.

Experiment 3: Infectivity of Concentrated Blood.—(*a*) A rabbit, dying, was killed by bleeding from the carotid artery. This rabbit had been injected subcutaneously with six 1-c.c. doses of a heavy suspension of the brain of a rabbit dying from fatal herpetic encephalitis (Strain 1). The injections were given daily, except for an interval of three days between the third and the fourth dose. Twelve days after the first injection, the rabbit showed paralysis of the hind legs, was excited and maintained a dorsal position. Three days after the symptoms developed, the animal was unable to rise and was in a semicomatose condition (in which condition it was bled to death). The blood was collected in a sterile flask containing beads and was defibrinated; it was then strained through sterile gauze to remove the fibrin clot and placed in a sterile petri dish. The petri dish, containing 25 c.c. of blood, was placed in a desiccator over calcium chlorid and a strong vacuum drawn for one and a half hours. The jar was then sealed and placed in the incubator at 38 C. (100.4 F.) for twenty hours. The blood now had the consistency of thick jam. As this concentrated mass was difficult to remove for the purpose of measuring the amount, an approximate estimate of 2 c.c. is given. This concentrated blood was abundantly inoculated into the scarified eye of a normal rabbit. By the third day, there was a marked keratoconjunctivitis, which became progressively worse. No cerebral symptoms developed, and by the twelfth day signs of improvement were noted. Thirty days after the infection, the conjunctivitis had subsided, the cornea, however, remaining turbid in the area of scarification, and two well circumscribed ulcers developing. Fifty-three days from the date of the infection, the animal appeared to be in good health; the cornea showed a minute ulcer and a slight opacity of the scarified area.

(*b*) *Series Transmission of Concentrated Blood Virus.*—During the active stage of the infection in the aforementioned rabbit, an attempt was made to transmit the infection to another rabbit. The result was a mild keratoconjunctivitis, with gradual resolution except for opacity at the site of scarification.

(*c*) *Effects of Diluted Concentrated Blood.*—The concentrated blood was diluted by adding 2 c.c. of normal salt solution. The object was to obtain a definite concentration. On measuring, it was found that there was a volume of 5 c.c., or a concentration of five times. Blood of this concentration was inoculated into a rabbit. A mild keratoconjunctivitis with gradual resolution developed; finally a slight opacity along the site of scarification of the cornea remained.

Summary.—Virulent herpetic virus exists in the blood of experimentally infected rabbits. It is possible to concentrate the virus to a degree of infecting a rabbit. The infectivity of the virus appears, however, to be reduced, as no cerebral symptoms were found to develop

after inoculation with concentrated blood, although the pus from the eye of any of the rabbits through which the strain was passed would produce fatal encephalitis.

FILTRABILITY OF HERPETIC VIRUS (STRAIN 1)

Although it is now generally thought that the cause of simple herpes is a specific virus, it has not yet been definitely settled whether or not it is a filter-passing one. Lowenstein [7] was not able to obtain positive "takes" when the herpetic virus was passed through a porcelain filter, but he expressed the opinion that the virus was, in all probability, a filter-passing one. Luger and Lauda [8] diluted the vesicular exudate with physiologic sodium chlorid, and filtered it for twenty-seven minutes (220 mm. water pressure) through a Nordmayer-Berkefeld candle, which had been tested previously with a pneumococcus suspension. The results with the filtrate were negative, whereas the unfiltered remains produced typical infection. Using a brain emulsion of an infected rabbit filtered through the same type of candle (90 mm. pressure 230 mm. water), a fatal result was produced in a rabbit inoculated intravenously with the filtrate. Levaditi and his co-workers [15] as well as Vegni [16] believe that the virus is filtrable. Perdrau [17] on the other hand, found that Chamberland filters L 1 and 2 will permit passage of such an organism as *B. prodigiosus*. This would seem to make the findings of Blanc and Caminopetros,[10] negative as they used an L 1 Chamberland candle, through which they found that the virus easily passes. Perdrau failed to produce experimental disease with the filtrate from a Massen porcelain candle.

FILTRATION EXPERIMENTS

The brain of a rabbit was removed in a sterile manner. This rabbit had received six daily subcutaneous doses of a heavy suspension of herpetic rabbit brain (animal killed when moribund) and had developed paralysis of the hind legs twelve days after the first injection and five days after the sixth injection. When the animal was dying (progressive involvement of the nervous system) it was chloroformed, and while under the anesthetic, bled to death, and the brain removed. The brain was emulsified and divided into two parts. One part was placed in 1 per cent. glucose hormone broth p_H 7.2 and the second part in 20 per cent. neutral glycerin. Aerobic and anaerobic cultures of these two suspensions, cultivated on hormone broth plus calf brain and blood agar plates, remained sterile after seventy-two hours. The two suspensions were placed in the refrigerator at 6 C. for twenty-four hours, to permit the virus to pass out from the brain material into the surrounding medium. They were then centrifugalized at a low speed to precipitate the coarse particles of brain

15. Levaditi, C.; Harvier, P., and Nicolau, S.: Ann. de l'Inst. Pasteur **36**:911, 1922.

16. Vegni, R.: Riforma med. **38**:270, 1922 (quoted by De Fano: J. Path. & Bacteriol. **46**:85, 1923).

17. Perdrau, J. R.: Ministry Health Reports on Lethargic Encephalitis, 1922.

and then passed through Mandler diatomaceous filters, tested 6 pounds. Aerobic and anaerobic cultures of these filtrates also remained sterile when incubated at 37.5 C. These unfiltered and filtered glycerin and glucose bouillon suspensions were then tested on animals as follows:

(*a*) Intracerebral inoculation of 20 per cent. glycerin filtrate.

Two-tenths cubic centimeter of the filtrate was inoculated into the brain of a normal rabbit. Thirteen days after the inoculation, the animal, which during the previous twelve days had appeared to be unaffected by the injection, was found lying on its side, head drawn back, with involuntary movement of its legs, and unable to rise when disturbed. It died the same day. Necropsy revealed marked congestion of the brain. A portion of this brain was removed under aseptic precautions and inoculated into a control animal. The control animal developed paralysis in twelve days, and was dead three days later.

(*b*) Corneal inoculation of 20 per cent. glycerin filtrate.

The cornea and conjunctiva of a rabbit were scarified and inoculated by flooding the conjunctival sac with the glycerin filtrate. The animal's eye remained normal.

(*c*) Intracerebral inoculation of unfiltered 20 per cent. glycerin suspension.

Two-tenths cubic centimeter of the unfiltered emulsion of the same brain used in the filtration tests was injected into the brain of a rabbit. Four days later, the animal showed opisthotonos, excitability and inclination to climb up the side of the cage. On the fifth day, it was found dead.

(*d*) Intracerebral inoculation of 1 per cent. glucose hormone broth filtrate.

Two-tenths cubic centimeter of this filtrate was injected into the brain of a rabbit. This animal remained normal over a period of twenty-eight days.

(*e*) Corneael inoculation of 1 per cent. glucose hormone broth filtrate.

The scarified cornea and conjunctiva of a rabbit was inoculated by flooding the conjunctival sac with this filtrate. The animal remained normal over an observation period of twenty days.

(*f*) Intracerebral inoculation of unfiltered 1 per cent. glucose hormone broth suspension.

The brain of a normal rabbit was inoculated with 0.2 c.c. of the unfiltered 1 per cent. glucose hormone broth emulsion of the same herpetic brain as was used for the filtrate. Nine days after the inoculation, the rabbit presented marked cerebral symptoms, opisthotonos, with the animal lying on its side, unable to rise. It became semicomatose the same day and died the following day.

SUMMARY

1. The preceding six brief experiments on the filtrability of a virulent herpetic virus obtained from a patient with recurrent herpes simplex shows as the chief result that the virus did pass through a Mandler diatomaceous filter of 6 pounds test as proved by the inoculation of a rabbit with the 20 per cent. glycerin suspension filtrate; the rabbit developing fatal herpetic encephalitis in thirteen days. On the other hand, the filtrate of a similarly made suspension in 1 per cent. glucose hormone broth failed to produce a positive inoculation take. The cultural tests on these filtrates were sterile both aerobically and anaerobically, proving that the filter candles were perfect.

2. The corneal inoculation of the filtrates were negative with both filtrates.

3. The control animals inoculated intracerebrally with the unfiltered suspension of the herpetic brain in 20 per cent. glycerin and in the 1 per cent. glucose hormone broth developed herpetic infection in four and nine days, respectively.

TABLE 2.—*Results of Inoculation with Strain 2**

No. of Passages	Material Inoculated	Method of Inoculation	Eye Symptoms	Cerebral Symptoms	Death	Reinoculation
4	Exudate from vesicle, then pus eye to eye	Corneal scarification	Marked on first and mild in last three passages	None	Lived	48 hours

* This virus was obtained, April 7, 1924, from the exudate of a severe spontaneous labial herpes febrilis.

TABLE 3.—*Results of Inoculation with Strain 3**

No. of Passages	Material Inoculated	Method of Inoculation	Eye Symptoms	Cerebral Symptoms	Death	Reinoculation
4	Same as Strain 2	Same as Strain 2	Mild at all times	None	Lived	48 hours

* This strain was obtained, April 6, 1924, from the exudate of a recurrent labial herpes simplex of fifteen years' duration, recurring once or twice monthly.

Strains 2 and 3 were carried through only four passages because the strains seemed to die out. The rabbits, however, were used for cross immunity tests against Strain 1.

ACQUIRED IMMUNITY

Rabbits previously infected with Strains 1 and 2 (mild strains which had never produced encephalitis and death), and which had recovered from their eye infections, were treated in the following manner:

1. One rabbit, inoculated with herpes virus Strain 1 into the scarified cornea of the same eye previously inoculated with a mild virus.

2. One rabbit, recovered from a mild herpetic virus infection, inoculated with herpetic virus Strain 1 into the scarified cornea of the opposite eye.

3. One rabbit, recovered from mild herpetic virus infection, inoculated intracerebrally with an emulsion of the brain of a rabbit just dead of herpetic (Strain 1) encephalitis.

Proper controls were likewise infected. Table 4 gives the details of these experiments.

Summary.—1. None of the rabbits that had recovered from a mild herpetic virus infection appeared to show the slightest immunity of the cornea when reinoculated with a strong herpetic virus, either in the same eye or in the eye opposite to that previously infected with the mild virus.

2. A rabbit, inoculated thirty-eight days previously with a mild herpetic virus (Strain 2), did not succumb to an intracerebral inoculation of the stronger virus (Strain 1), whereas the control rabbits developed encephalitis in eight and fourteen days, respectively.

3. A rabbit inoculated and recovered fifty days previously from a mild herpetic virus infection (Strain 2) developed keratoconjunctivitis when inoculated with the stronger Strain 1, but did not develop encephalitis. The control rabbit developed cerebral symptoms in eight days, and was dying on the ninth day.

TABLE 4.—*Results of Immunity Tests* *

Primary Virus	Time Interval between Original Infection and Immunity Test	Eye First Infected	Eye Tested for Immunity	Brain Tested for Immunity	Result of Inoculations with Strain 1		
					Corneal Symptoms	Brain Symptoms	Dead, Killed, Lived
Strain 2	50 days	Left	Left	—	Marked keratoconjunctivitis in 48 hours	None	Alive after 143 days
Strain 2	40 days	Right	Left	—	Marked keratoconjunctivitis in 72 hours	6 days	Dead after 7 days
Strain 2	38 days	Left	—	Yes	—	None	Alive after 143 days
Strain 3	50 days	Left	Left	—	Marked keratoconjunctivitis in 48 hours	7 days	Dead after 8 days
Strain 3	29 days	Right	Left	—	Mild keratoconjunctivitis in 72 hours, marked in 96 hours	12 days	Dead after 13 days
Strain 3	38 days	Left	—	Yes	—	8 days	Dead after 8 days
Control corneal inoculation	Normal rabbit	—	Left	—	Marked keratoconjunctivitis in 48 hours	8 days	Killed after 9th day
Control brain inoculation	Normal rabbit	—	—	Yes	—	8 days	Dead after 13th day
Control brain inoculation	Normal rabbit	—	—	Yes	—	14 days	Dead after 16th day

* Infected, May 27, 1924. Scarified corneas were inoculated with pus from eye of rabbit presenting marked keratoconjunctivitis. Brain inoculation made by trephining and injecting 0.1 c.c. emulsified brain of rabbit killed previous day while in coma from herpetic encephalitis. Brain preserved in sterile 50 per cent. glycerin in refrigerator at 6 C. over night.

4. Three rabbits previously infected with a mild herpetic virus, Strain 3, developed a keratoconjunctivitis with cerebral symptoms in eight, thirteen and eight days, respectively, after inoculation with the strong herpetic virus, Strain 1. Apparently, no immunity had been produced by the previous herpetic infection.

INDUCED IMMUNITY

EXPERIMENT 1.—Can rabbits be immunized to herpetic disease by the subcutaneous injections of an emulsion of herpetic brain, the presence or absence of an induced immunity to be later tested by inoculation into the scarified cornea?

Technic: The entire brain of a rabbit showing pronounced symptoms of herpetic disease of the central nervous system was emulsified in 50 c.c. of

a 20 per cent. glycerin solution. This made approximately a 40 per cent. suspension of brain material (the estimate is made on the average weight of a rabbit's brain, 20.5 gm.).

All of the rabbits (four in number) were injected subcutaneously with 1 c.c. of this emulsion daily until six injections had been given.

Table 5 gives the details of the results.

TABLE 5.—*Results of Subcutaneous Injections of an Emulsion of Herpetic Brain*

Rabbit No.	Dates of Subcutaneous Injections						Results
	April 17	April 18	April 19	April 20	April 21	April 22	
1	1 c.c.	1 c.c.	1 c.c.	1 c.c.	1 c.c.	1 c.c.	Developed herpetic disease in 12 days; comatose on 13th day; killed
2	1 c.c.	1 c.c.	1 c.c.	1 c.c.	1 c.c.	1 c.c.	Herpetic disease on 16th day; comatose on 18th day; killed
3	1 c.c.	1 c.c.	1 c.c.	1 c.c.	1 c.c.	1 c.c.	Herpetic disease on 11th day; comatose on 12th day; killed
4	1 c.c.	1 c.c.	1 c.c.	1 c.c.	1 c.c.	1 c.c.	Remained normal (observation for 18 days)
5	Brain emulsion inoculated intracerebrally to determine presence of virus						Died from herpetic encephalitis in 10 days

Goodpasture and Teague[18] had not been able to produce herpetic disease in rabbits by subcutaneous injections of the living virus. It had been planned that if our rabbits did not develop herpetic disease from the subcutaneous injections, their corneas were to be scarified and inoculated with the pus from an active corneal infection in order to determine the presence or absence of immunity. Accordingly, the corneas of both eyes of the only surviving rabbit were scarified and only the left eye inoculated. Within forty-eight hours, there was a marked keratoconjunctivitis. By the fifteenth day, improvement in the condition of the eye had commenced. By the twenty-first day, the animal was apparently normal, except for the presence of a mild keratoconjunctivitis and the presence of two well defined scars of ulcers that had been present. Thirty-six days later, only a slight gray dot on the cornea showed where the ulcers had been.

In order to determine whether or not this eye had now developed a local immunity, it was reinfected at this time in the usual manner. A fairly marked keratoconjunctivitis developed, which showed signs of subsidence within a week, and which was normal by the thirteenth day.

Summary.—1. Seventy-five per cent. of the animals injected subcutaneously wtih a 40 per cent. suspension of herpetic brain developed herpetic encephalitis within from twelve to sixteen days.

2. Inoculation of the cornea of the one surviving rabbit with active virus was followed by a prolonged keratoconjunctivitis and ulcer formation. No encephalitis developed, although the control animals (those used to carry the strain) developed encephalitis usually within ten days, and died.

3. Reinoculation of the previously infected eye of the rabbit referred to above resulted in the development of a marked keratoconjunctivitis, with rapid recovery to normal within thirteen days.

18. Goodpasture, E. W., and Teague, O.: J. M. Res. **44**:191, 1923.

EXPERIMENT 2.—Can rabbits be immunized by subcutaneous injections of herpetic brain prepared as a vaccine according to Terrell's method of preparing antirabic vaccine?[19]

Technic: The brain of a rabbit dying from herpetic encephalitis was used. One gram of the medulla and 1 gm. of the pons (parts in which we and others have definitely ascertained that the infection is most highly concentrated when the eye is infected primarily) were placed in a mortar, thoroughly triturated, and 25 c.c. of sterile distilled water slowly added, then a second 25 c.c. of sterile distilled water containing 1 gm. of pure phenol (carbolic acid) crystals.

The 50 c.c. of brain suspension was placed in the incubator at 37.5 C. for twenty-four hours, for the purpose of killing the virus. At the end of the twenty-four hour period, the volume was brought up to 200 c.c. with sterile distilled water, giving a final dilution of medulla and pons substance of 1:100 or 1 per cent. and of phenol 0.5 per cent. This vaccine was then used for subcutaneous injections, details of which are given in Table 6.

TABLE 6

Rabbit No.	Weight in Gm.	Dose Every Second Day	Number of Doses	Interval between Last Dose and Corneal Test	Results		
					Corneal Symptoms	Cerebral Symptoms	Death, Killed or Lived
1	1,490	2 c.c.	6	9 days	Marked keratoconjunctivitis in 48 hours	7 days	Death on 11th day
2	1,730	2 c.c.	6	9 days	Marked keratoconjunctivitis in 48 hours	7 days	Death on 9th day
3	1,480	2 c.c.	12	8 days	Marked keratoconjunctivitis in 48 hours	9 days	Killed on 9th day
4	1,560	2 c.c.	12	8 days	Same in 72 hours	None; death very sudden	Died on 6th day
5	1,660	2 c.c.	18	7 days	Same in 72 hours	Lost 700 gm. in weight during course of treatment; in poor physical condition at time of test; died 4 days after test	
6	1,640	2 c.c.	18	—	This animal lost considerable weight during the treatment; it died 48 hours after last dose of vaccine		
7, 8 and 9	Three controls which developed marked keratoconjunctivitis, cerebral symptoms of herpetic encephalitis in 7 days; death in 8, 10 and 11 days, respectively						

The plan of the experiment was to give six rabbits daily injections of 2 c.c. each of this vaccine. Two rabbits were to receive six injections; two were to receive twelve injections and two were to receive eighteen injections.

Summary.—1. Rabbits which had received as many as twelve subcutaneous injections of a 1 per cent. suspension of killed herpetic brain virus in 2 c.c. amounts acquired neither a local nor a general immunity, as evidenced by the development of encephalitis on subsequent corneal herpetic infection.

2. Eighteen subcutaneous injections of 2 c.c. reduced the vitality of one rabbit to the point of death, while the second rabbit, on corneal inoculation, developed a keratoconjunctivitis but died before the development of cerebral symptoms.

19. Kolmer, John A.: Infection, Immunity and Biologic Therapy, Philadelphia, W. B. Saunders Company, Ed. 3, 1923, p. 789.

EXPERIMENT 3.—Can rabbits be immunized with living herpetic brain virus prepared in the same manner as Terrell's antirabic vaccine except that the virus is not killed?

Technic: Part of the suspension prepared for the previous experiment was used for this experiment. The vaccine was made in the same manner except that, in order not to kill the virus, the suspension was not incubated, and no phenol (carbolic acid) was added, with the exception of a final addition to the point of 0.5 per cent. as a preservative. The vaccine, if it may be called that, was constantly kept in the refrigerator at 6 C.

Two rabbits were used: One rabbit received one dose of 2 c.c. of this living 1 per cent. emulsion of herpetic brain and the other rabbit received two injections, six days apart. Their immunity was tested by corneal inoculation.

Table 7 gives in detail the results of this experiment.

TABLE 7.—*Results of Experiment 3*

Rabbit No.	No. of Injections	Dosage	Interval between Doses and Immunity Test	Results		
				Corneal Symptoms	Cerebral Symptoms	Died, Killed or Lived
1	1	2 c.c.	18 days	Marked keratoconjunctivitis in 24 hours	7 days	Died 14 days
2	2	2 c.c.	12 days	Marked keratoconjunctivitis in 24 hours	7 days	Alive at end of 104 days

Rabbit 2.—The history of Rabbit 2 (Table 7) is of especial interest. By the ninth day, the animal was not able to rise; the head was drawn back; it neither ate nor drank, and remained in this state for three days. On the twelth day, the animal appeared to be somewhat stronger, made efforts to rise and at times succeeded in attaining a sitting position. By the fifteenth day, it had assumed a semidorsal position and showed recovery of appetite. By the eighteenth day, the animal was able to rise and lie down at will, although with difficulty. Its appetite was good, but the animal was emaciated. Gradual recovery took place from now on. One hundred and four days after the infection, the animal was in good physical condition, except for a tendency to lean its head toward the left side (left eye infected) and a slightly turbid cornea.

Summary.—1. One subcutaneous injection of a 1 per cent. suspension of living herpetic brain virus did not confer sufficient immunity to withstand a later corneal inoculation.

2. Two subcutaneous injections of the same vaccine, 2 c.c. to the dose at an interval of six days, did not prevent the development of a herpetic keratoconjunctivitis and herpetic encephalitis. The encephalitis was eventually followed by recovery, whereas the control animals injected at the same time died of a typical herpetic encephalitis.

HERPETIC ANTIBODIES

In determining the presence or absence of antibodies, the method of Levaditi-Landsteiner (used by these authors in the study of the mechanism of immunity in Heine-Medin disease) was used. Do animals

injected intracerebrally with a mixture of an emulsion of herpetic brain and the serum of supposedly immune and of normal rabbits succumb to herpetic disease?

Technic.—The blood of animals that had been formerly infected and had recovered, or of rabbits that had been vaccinated, was collected in sterile test tubes. The clear unheated serum was mixed with a definite amount of herpetic brain emulsion, incubated at 37.5 C. for half the tests, and another portion placed in the refrigerator at 6 C. for twenty-four hours, for the other

TABLE 8.—*Results of Tests with Herpetic Antibodies*

No.	Source of Serum	Material Injected Intracerebrally	Period of Incubation of Serum and Herpetic Brain Mixture before Inoculation	Time Interval between Vaccination or Infection and Date of Bleeding	Results		
					Eye Symptoms	Cerebral Symptoms	Dead, Killed or Lived
1	Rabbit with old herpetic infection	Serum and herpetic brain	4 hours at 37.5 C.	23 days	None	None	Alive, 36 days
2	Rabbit with old herpetic infection	Serum and herpetic brain	24 hours at 6 C.	23 days	None	None	Dead, 4 days
3	Rabbit with old herpetic infection	Serum and herpetic brain	4 hours at 37.5 C.	12 days	None	None	Dead, 24 hours
4	Rabbit with old herpetic infection	Serum and herpetic brain	24 hours at 6 C.	12 days	None	None	Alive, 36 days
5	Rabbit that had received 6 doses of living virus	Serum and herpetic brain	4 hours at 37.5 C.	98 days	None	15 days	Dead, 18 days
6	Rabbit that had received 6 doses of living virus	Serum and herpetic brain	24 hours at 6 C.	98 days	None	18 days	Dead, 21 days
7	Received 2 doses of living virus	Serum and herpetic brain	4 hours at 37.5 C.	75 days	None	None	Alive, 36 days
8	Received 2 doses of living virus	Serum and herpetic brain	24 hours at 6 C.	75 days	None	4½ days dull, no paralysis	Dead, 5 days herpes (?)
9	Normal rabbit	Serum and herpetic brain	4 hours at 37.5 C.	.....	None	None	Alive, 36 days
10	Normal rabbit	Serum and herpetic brain	24 hours at 6 C.	.....	None	None	Alive, 36 days
11	Normal rabbit	Serum and herpetic brain	4 hours at 37.5 C.	.....	None	19 days	Dead, 23 days
12	Normal rabbit	Serum and herpetic brain	24 hours at 6 C.	.....	None	25 days	Dead, 28 days
13	.....	Salt solution of herpetic brain	4 hours at 37.5 C.	.....	None	—	Dead, 24 hours
14	.....	Salt solution of herpetic brain	24 hours at 6 C.	.....	None	6 days	Dead, 7 days

tests. The scarified cornea and the brains of normal rabbits were both inoculated. The blood serum of normal rabbits as well as physiologic sodium chlorid were used as controls. The mixture of serum and brain emulsion was prepared as follows: The medulla, pons and surrounding parts of brain, parts where it has been demonstrated that the virus is most abundant, were triturated in a mortar, sufficient normal salt solution being added to make it possible to draw up the mixture into a wide mouthed pipet. Two-tenths cubic centimeter of this emulsified brain and 0.2 c.c. of the serum to be tested were mixed in a test tube and incubated as already noted.

The results of the tests are given in detail in Table 8.

Summary.—As is seen, the results of this experiment are not satisfactory. It is possible that the factor of individual immunity, or the quantity of virus necessary to infect, or both, play a considerable part in an experiment in which the volume of 0.2 c.c. is the maximum that can be safely injected. Nevertheless, it appears probable that some of the rabbits possessed an immunity (That is, their blood serum contained some immune bodies) over the normal rabbits and the plain salt solution control.

SERUM DIAGNOSIS OF HERPETIC DISEASE

Besides a desire to complete our studies, it was thought that complement-fixation tests might be of special interest. Accordingly, the serums of rabbits, vaccinated or in an active stage of the infection, were examined for herpetic reagin by means of Kolmer's new standardized technic.

Preparation of Antigen.—The brain of a rabbit infected by corneal inoculation ten days previously and dying from herpetic encephalitis was placed in 96 c.c. of physiologic sodium chlorid, to which were added 4 c.c. of a 5 per cent. solution of phenol. This was shaken for two hours, incubated over night, then centrifugalized and titrated for its anticomplementary activity by the new method. The serums used and the results of the tests (conducted with one-third the anticomplementary unit of antigen) are given in Table 9. Both heated and unheated serums were tested.

TABLE 9.—*Complement-Fixation Tests*

Serums Obtained	Time Interval between Vaccination or Infection and Bleeding	Unheated Serums								Heated Serums							
							S. C.								S. C.		
		1:20	1:40	1:80	1:160	1:320	1:20	1:40	1:80	1:20	1:40	1:80	1:160	1:320	1:20	1:40	1:80
Rabbit which had received two doses of living vaccine plus positive "take" when tested for immunity	44 days	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Same, except six doses of living virus given	67 days	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Rabbit infected first with Strain 2 and later with Strain 1	77 days	±	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Intracerebral inoculation with concentrated blood from rabbit with herpetic disease	52 days	4	3	—	—	—	—	—	—	4	—	—	—	—	—	—	—
Rabbit dying from herpetic encephalitis	11 days	3	1	—	—	—	—	—	—	2	—	—	—	—	—	—	—
Rabbit dying from herpetic encephalitis	10 days	±	±	—	—	—	—	—	—	4	±	—	—	—	—	—	—
Rabbit dying from herpetic encephalitis	7 days	4	—	—	—	—	—	—	—	1	—	—	—	—	—	—	—
Normal control 1	—	4	4	—	—	—	—	—	—	4	—	—	—	—	—	—	—
Normal control 2	—	1	3	±	—	—	—	—	—	4	—	—	—	—	—	—	—

The foregoing tests were performed by Dr. John A. Kolmer who gives the following report:

I interpret these tests as negative, conclusively negative, since the reactions were done by a very sensitive method which brought out the nonspecific reaction with 0.025 c.c. of serum (0.5 of 1:20).

CONCLUSIONS

1. Herpetic disease in rabbits is a generalized infection.

2. The filtrability of the herpetic virus varies with the suspending medium.

3. The local (tissue) immunity produced by herpetic virus is not absolute. The severer the infection (or the more virulent the virus without causing death), the greater the local immunity.

4. Mild herpetic virus infections do not protect against severe herpetic virus infections.

5. Slight herpetic antibody production appears to occur in herpetic disease.

6. Complement-fixing substances do not develop in herpetic disease.

7. Subcutaneous injections of the virus (living or dead) lead to the production of little or no immunity to herpetic disease.

STUDIES ON HAIR

WITH SPECIAL REFERENCE TO HYPERTRICHOSIS

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III. GENERAL CHARACTERISTICS OF HUMAN HAIR

Man is unique among the mammals in his complete lack of tactile hairs. So far as is known, every other mammal possesses them. They are the first to appear in the embryo and persist after all others have been lost through disease or phylogenetic reduction. But with man they are found, if at all, only as transient embryonic rudiments. This absence of true tactile hairs may be mentioned as one of the few qualitative differences between man and all other mammals. In most respects, human hair conforms fairly well in character and distribution to the hair of other members of the class, especially the anthropoid apes.

HAIRLESS REGIONS OF THE BODY

The human species is by no means the most nearly hairless animal, for, as already mentioned, most cetaceans and many representatives of other orders are less well provided. But in man, the great majority of hairs never develop beyond more or less rudimentary down. This peculiarity is a rather highly characteristic human trait since, with few if any exceptions, other mammals are relatively poorer in down than in the coarser forms of hair. The total amount of really hairless skin in man is small, being confined to a few special areas. Hair does not normally occur on any invaginated ectoderm except close to the nostrils and in the external auditory meatus. It has been reported in a number of instances as growing from various mucous membranes, but most, and probably all, these cases may be attributed to the presence of dermoid cysts. The other regions in which it is characteristically absent are the margin of the lips, areolae of the nipples, the umbilicus, the immediate vicinity of the anal and urogenital openings, including the labia minora and prepuce, the soles, the palms, and the terminal parts of the fingers and toes. The hairless area on the foot extends well up on both the lateral and medial margins, including the lower part of the fossae between the malleoli and Achilles tendon behind, and the terminal segments of the toes and second interphalangeal joints in front. The hairless region of the hand is comparable, morphologically, to that of the foot, the bare region of the heel being apparently represented by a more or less triangular area extending several centimeters along the flexor surface

of the forearm somewhat to the ulnar side. As with the toes, the skin of the fingers back to and including that over the terminal interphalangeal joints is without hair. It is doubtful, too, if hair ever occurs over the proximal interphalangeal joints of the fingers or four lateral toes.

The regions indicated in the preceding paragraph as hairless are believed to be entirely free from hair or hair rudiments in all races and at all age periods. There is no indication that this pecularity is in any way modified in disease or in cases of the most marked hypertrichosis.

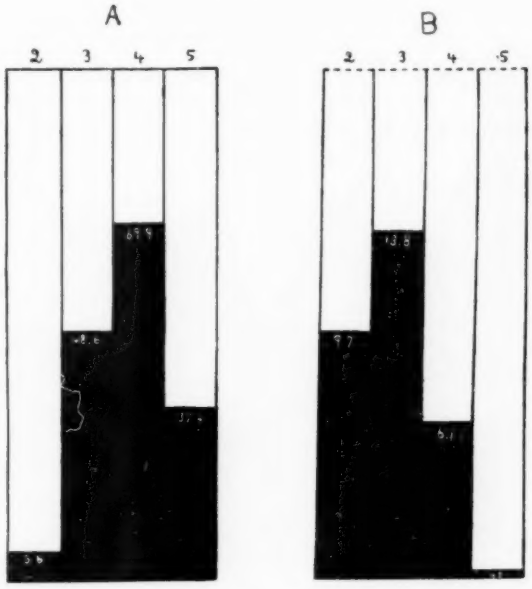

Fig. 25.—The frequency of the presence and absence of hair on the middle segments of the digits in 442 white soldiers (Am. Jour. Phys. Anthrop.) *A*, represents the fingers; *B*, the toes. The columns headed 2, 3, 4 and 5 indicate the digits commonly designated by those numbers. The black areas show the percentage of cases in which the respective digits had hair on their middle segments, the light areas the percentage which lacked it. *B*, corresponds to the base of a polygon ten times as high as *A*.

In certain persons, an extension of the hairless areas to cover the middle segments of the fingers and toes has been reported by Danforth. In these cases, which include nearly all negroes and Indians that have been examined, as well as about one-fourth of white Americans, the absence of hair is not merely apparent but real, as shown by embryologic and histologic studies. This absence of hair from the middle segments may involve all the digits (except the thumb and great toe, which are presumed to lack a middle phalanx) or it may extend to only part of

them. Of the fingers, the index is the one which most often has no hair on its middle segment. This is followed in turn by the little, middle and ring fingers. It is noteworthy that if hair is absent from the middle segment of the ring finger it is almost invariably absent from the corresponding segments of all the others. In the foot, where the frequency of absence of hairs on the middle segments of the toes is in the sequence of the fifth, fourth, second, third, there is a similar relation in reference to the third digit. In the white race, these areas are bare on the toes about ten times as frequently as on the fingers (Fig. 25). The middle segments of the fingers and toes, which may probably be regarded as morphologically only two regions, and those homologous, represent the only parts of the body which, so far as has been ascertained, show any present phylogenetic tendency toward an increase in the amount of hairless skin.

REDUCTION IN HAIRINESS

Other parts of the body are covered with hair in greater or less abundance. For given regions, there may be a wide range individually and racially in the degree of hair development, but whether or not the total number of hairs to the unit area varies appreciably seems to have been ascertained for only two regions, the face and the fingers. Dr. Trotter states that no constant sexual or racial difference in the actual number of facial hairs has been found. In this region, the differences in apparent hairiness of different persons seems to depend primarily on the size of hairs rather than on any marked variation in their number. A study of facial hair taken by itself would lead one to suspect that if the human race is becoming less hairy it is doing so not by a reduction in the number of hair follicles formed, but by a more and more complete suppression of the growth of the hairs that are present. There is considerable evidence pointing in this direction, and one might easily imagine that this is the only process involved were it not that study of digital pilosity indicates that in some parts of the body there may be other factors. On the middle segments of the fingers, the actual numbers of hairs in a definite area varies widely, as has been determined by careful examination of the living and by microscopic sections. Here one may find on the middle part of the ring finger, for example, of one person a single well developed hair with no trace of any other follicles, while in exactly the same place in another subject there may be as many as twenty or twenty-five hairs of various sizes.

The two contrasted types of hair reduction, involving in the one case actual diminution in the number of follicles and in the other a deficiency in the growth of the individual hairs might be referred to as actual and apparent reduction. The two types have not been adequately studied. They may occur more or less independently in the white race but are

associated in the negro and Indian, a fact that is possibly of some significance. Whether actual reduction as compared with the apes has occurred in other parts of the body than the fingers and toes, is open to question. A comparative microscopic count of the hairs of human fetuses at the age of about 6 months and of several fetal apes and monkeys of approximately the same stage of development was made by Meyer-Lierheim, the results of which are summarized in Table 1. It appears from these figures that man has more numerous hairs on his head than either of the three anthropoids examined and more on his back than either the chimpanzee or the gibbon. As compared with the macaque man seems to have considerably less hair, but a square centimeter of surface on a human fetus represents a comparatively much smaller area than does a square centimeter of surface in the fetus of a medium sized monkey, so even here the relative difference may be small or even in favor of man. There can be no doubt, however, that as compared with many of the lower mammals the human species has a considerably reduced number of hairs. It has not been established that

TABLE 1.—*Comparative Microscopic Count of Hairs of Human Fetuses and Fetal Apes and Monkeys of Same Stage*

Region Examined	Number of Hairs to a Square Centimeter of Skin				
	Man	Orang	Chimpanzee	Gibbon	Macaque
Head	880	383	400	546	1,240
Back	688	187	420	440	1,406

this reduction was brought about primarily through an elimination affecting exclusively some special type of hair, such as the bristle or awn. The tactile hairs have disappeared, but as to the exact nature of other losses, nothing definite is known. The problem is complicated by possible independent factors making for the partial suppression of hair growth without necessarily any elimination of hair follicles. From the point of view of comparative morphology, this is a matter requiring further study.

HAIR OF THE FETUS

In development, the first definite hair rudiments in the human embryo appear on the forehead at the end of the second or during the third month of intra-uterine life, and by the end of the fourth month very fine, soft, and unpigmented hairs mark the region of the eyebrow and its immediate vicinity. Only slightly later (in fetuses of 120 mm., according to Frédéric) hair appears on the upper lip and scalp, followed at once by hair on the lower lip. During the next two months, the number of hair rudiments increases and their distribution spreads, the backs of the hands and feet becoming hairy, according to Friedenthal, at about the

end of the sixth month. It is frequently stated in the textbooks and maintained by Spuler that new follicles continue to appear even after birth, but owing to the natural wide variation in the size of closely adjacent follicles, it is easy to mistake a tangential section or a small follicle for a newly developing follicle, and there may be some question as to the accuracy of these statements. Scars usually fail to develop hair follicles, but substitution tissue following a transplant, at least in animals, may have follicles which, however, are possibly drawn on from the periphery. Whether or not this supposed late appearance of new follicles is a reality is an important question that awaits more critical investigation.

That the eyebrows should be the first hairs to appear in the human fetus and that they should be almost immediately succeeded by hairs on the upper lip are points of considerable interest, since it is precisely in

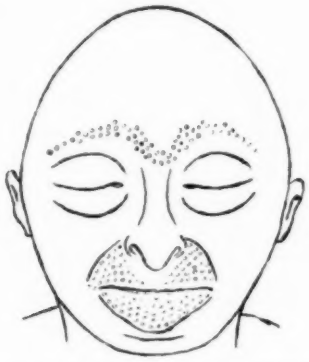

Fig. 26.—Gibbon embryo of 5 cm. to show developing sinus hairs (Frédéric).

these places and in this order that the first sinus hairs appear in fetal apes. The fact that the eyebrows and the mustache occupy comparable positions to tactile hairs in the apes, that they are the first hairs to appear in the embryo, and have certain superficial resemblances (Fig. 26) has been used as an argument for considering these particular human hairs as morphologically comparable to the sinus hairs of lower forms. This rather widespread view has not been borne out by careful investigation. Frédéric's study of developmental stages showed that the hairs of the mustache and those of the eyebrows, both of old men and of fetuses, have nothing in common with sinus hairs except their early appearance and topographical position. There is nothing in the follicular structure of human hairs to suggest kinship with tactile hairs. Frédéric himself concluded, as a morphologist, that it is not altogether impossible that the eyebrows and mustache have descended from sinus hair but that there is no well founded evidence that such is the case. From the point

of view suggested earlier in this book, the hairs of the eyebrow or mustache might be thought of as perhaps partially homologous with sinus hairs, development of the different forms being due to germinal complexes having some, but not all, factors in common.

That the human species has not entirely lost the tendency to produce tactile hairs has been maintained recently by Broman, who finds on the

Fig. 27.—Right forearm of a 28.5 mm. human embryo (Broman). The elevations on the ulnar side above the wrist are interpreted as indication of a transient tendency toward the formation of tactile hairs, since they occur at a point where such hairs are developed in the cat (Fig. 28).

arm of a 28.5 mm. embryo (probably about seven weeks old), little elevations (Fig. 27) at a site corresponding to the position of "carpal vibrissae" of certain other forms as, for example, the cat (Fig. 28). Similar elevations are found on the nose and face. These ephemeral structures Broman considers as transient manifestations of vestigial

tactile hairs. Should his observations be confirmed, they would have considerable interest from a phylogenetic point of view.

STAGES IN DEVELOPMENT OF FETAL HAIR

Apart from the question of presence or absence of sinus hairs or their homologues, human hair development presents little of special interest as compared with that of other animals. Stöhr, some of whose figures are copied herewith, divides the process of development of fetal hair into four stages.

His initial period or "hair germ" stage covers the period from the first indication of thickening in the ectoderm to the formation of a compact nodule of cells projecting into the corium. Figure 29 is from a

Fig. 28.—Left forearm of a 17 mm. cat embryo (Broman). The elevation on the ulnar side above the wrist is the site of tactile hairs which develop later.

developing follicle near the end of the first stage. At this time a slight suggestion of asymmetry in the follicle may be noted, indicating its future obliquity. Only the ectoderm is concerned in the initiation of follicle growth, but by the end of the first stage the corium shows some reaction in the form of the accumulation of nuclei beneath the epithelial downgrowth.

The second period in hair development Stöhr calls the "hair peg stage." This begins when the epithelial downgrowth assumes a more or less cylindrical form, and continues to the time when its deep extremity is indented by the developing hair papilla. A follicle toward the end of

the second stage is shown in Figure 30. By this time, several indications of organization are apparent. The "hair peg" shows some differentiation into neck and bulb but only slight specialization of the cells. The regions of the future sebaceous gland and the epithelial bed are vaguely indicated. Nevertheless, the whole structure is still a solid mass of cells, the core being filled and continuous with a strand of somewhat specialized cells indicating the site of the future subepitrichial hair canal. The surrounding mesenchyme is organizing into a connective tissue sheath which is especially thickened just beyond the end of the epithelial downgrowth. A few round nuclei close to the latter represent the true hair papilla. Several nuclei in the mesenchyme below the rudiment of the sebaceous gland may probably be interpreted as forerunners of the arrector pili muscle.

Then follows the third stage, which lasts until the hair proper appears in the follicle. In this stage, illustrated by Figure 31, the "hair peg" is

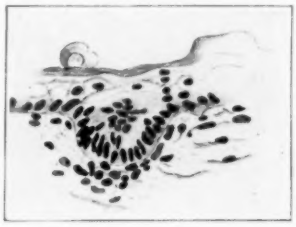

Fig. 29.—Skin of the forehead of a 5 months fetus showing early stage in the development of hair. (After Stöhr).

dilated at the end into a bulb encasing a well developed connective tissue papilla. The transition from the second to the third stage must be effected rapidly, since it is only exceptionally that one sees a developing follicle in the intermediate condition. In the third stage, one finds a more marked differentiation in the follicle. The sebaceous gland, not well shown in the figure, is further developed, and the epithelial bed, supposed to be the source of new hair shafts following molting later on, has attained to considerable proportions. In the bulb, indications of both Henle's and Huxley's layers are present, and the cells from which the hair itself will form are definitely indicated. The connective tissue sheath and the hyaline membrane, derived in part from the mesenchyme and in part from epithelium, are now present. The arrector pili muscle is definitely indicated, except in connection with follicles for hairs which characteristically lack it. "Arrector muscles are absent from the lanugo of the nose, cheeks and lips, and also from the eyelashes (cilia) and nasal hairs (vibrissae)." In the third stage, the axis of the "hair peg" is still filled with cells.

The fourth period, designated as the "sheathed hair stage," begins with the definite appearance of the hair shaft at the end of the third stage and continues until the hair ruptures, pushing its tip above the surface of the skin. This stage is characterized by the breaking down of cells in the axis of the follicle and under the epitrichial layer of the epidermis forming the hair canal. The phenomenon appears before the hair itself is much developed and considerably in advance of any apparent need for such an opening. At the same time, there is a partial degeneration of the inner epithelial sheath followed by superficial corni-

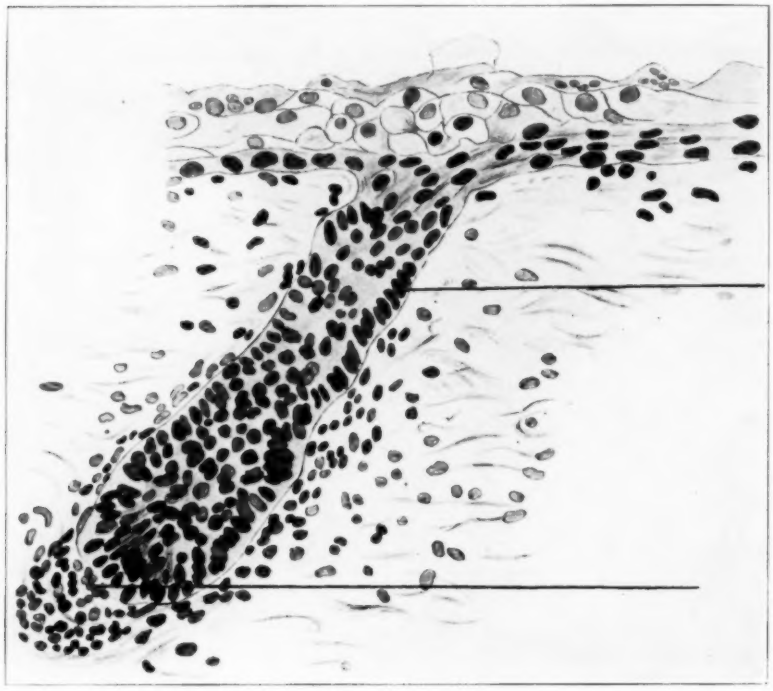

Fig. 30.—A hair follicle at about the end of the second stage. Magnification about 300 (after Stöhr). *P*, anlage of papilla; *S*, first indication of the sebaceous gland.

fication and the formation of the cuticular layer. This stage is represented semidiagrammatically in Figure 32. When the tip of the growing hair reaches the epitrichium, it is deflected horizontally in the hair canal. Continued growth finally results in a bowing of the distal part of the hair shaft and a consequent rupture of the epitrichium.

THE LANUGO

The first hairs are formed and reach a considerable development during the period extending from the third to the seventh month of intra-

uterine life. They are fine, slender, slightly, if at all, pigmented, and with some of the characteristics of wool. Many of them are longer than the down by which they are subsequently replaced. The cortical scales are large, and a medulla is lacking. It will probably make for greater clarity if the term lanugo is restricted to hair of this type. At their first

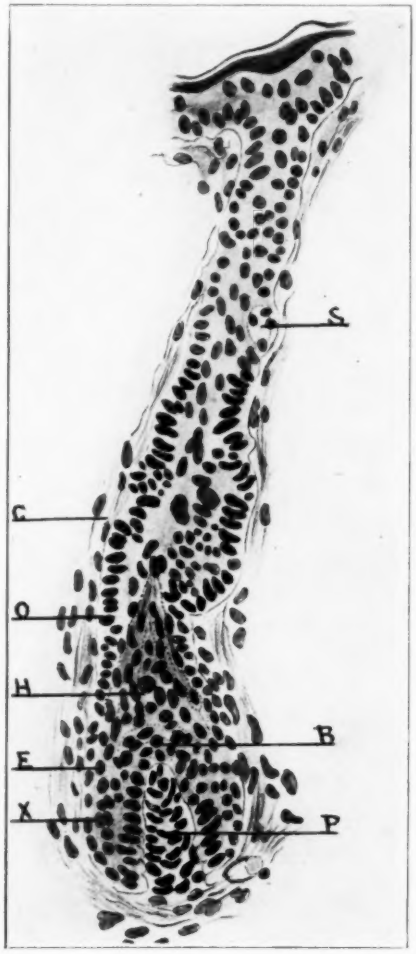

Fig. 31.—Hair follicle from the back of the nose representing the third stage. Magnification about 300 diameters (after Stöhr). *C*, connective tissue sheath; *O*, outer epithelial sheath; *H*, hair rudiment; *E*, Henle's layer; *X*, Huxley's layer; *S*, sebaceous gland (only indicated); *B*, bulb; *P*, papilla.

appearance, these hairs occur singly, but soon many of them are found in groups of two or rarely five as a result of two or more new hairs forming about an older one. Most, and perhaps all, of the first hairs are shed before birth. The process of shedding (Fig. 33) has been

worked out in detail by several investigators and consists in a series of changes in the follicle initiated by a cessation of growth in the hair bulb and a more or less complete atrophy of the papilla. There is no certainty that the process is the same in fetus and adult. It is doubtful that the first hairs have any function. One rather fanciful suggestion that

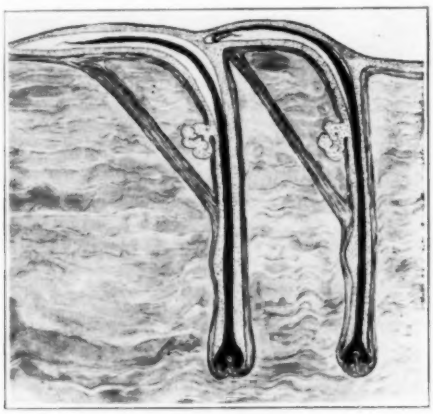

Fig. 32.—Diagrammatic representation of hairs immediately before rupture. The young hairs are still covered by the epitrichial layer which is on the point of rupturing.

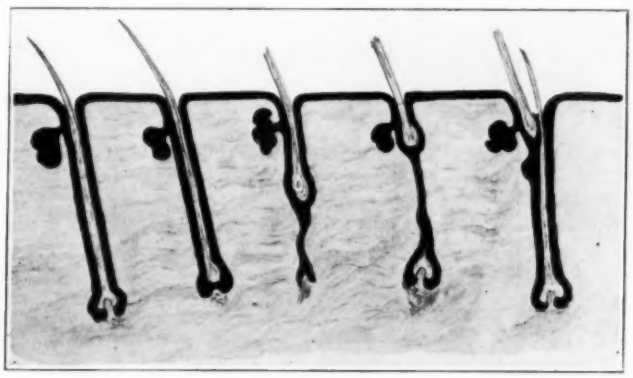

Fig. 33.—Diagram of stages in maturation and replacement of fetal hair. Epithelium, sebaceous glands and epithelial sheath in the follicle are solid black; connective tissue is gray.

has been advanced is that since they are shed into the amniotic fluid they should be regarded as a form of excretion. Another possibility, more acceptable from a morphologic standpoint, is that they represent a phase of the recapitulation process. Even this is perhaps rather far fetched,

and it seems quite as satisfactory to regard this first feeble production of hair as the early expression of a function that has not reached its height.

By the time of birth, the hairs of the eyelashes, eyebrows and scalp, while still soft and partaking more or less of the character of lanugo, show a much more vigorous growth than did the earlier generations in these regions. Particularly in dark infants, the hair shafts may be well pigmented at this time. Frequently, there is also present at birth a considerable amount of conspicuous hair in other places, such as the face, ears, body and especially the shoulders. This persistent lanugo on the body, along with most or all of the hair of the scalp, is shed during the first few months. That of the eyebrows and scalp is replaced in general by the coarser and more typical hair of those regions, while over the rest of the body the replacing hair, if not finer, is at least relatively shorter, and after a few generations resolves itself into the typical form of human down hair, which is fine, short, generally unpigmented, and usually without medulla. There is little precise information on the growth, duration of life and sequences in stages of the hair during early childhood.

AGE CHANGES IN THE PILARY SYSTEM

The gradual changes that take place in the hairy covering during late fetal life and childhood are continued through the period of maturity to old age. This is especially true of certain persons in whom, as Friedenthal has remarked, the pilary system seems never to reach a stage of equilibrium. Particularly in men, the hair over the body, in the eyebrows, on the face, in the nostrils and on the ears increases and becomes more apparent long after adult life has been reached. In both white and negro women, Trotter found a steady increase in the average length and diameter of hairs of the lip and cheek from youth to senility. It is a strange aspect of these changes that only a part of the hairs of any region are affected, many of them remaining as small as those of the fetus.

The first few generations of hair may be referred to as the primary hair. This is the covering of the fetus and to a large extent of the new-born. It is customary, but perhaps somewhat confusing, to class together as "wool" the primary hair of the fetus and the down of the adult. While the two forms have much in common, small dimensions, deficient pigment, small or absent medulla, relatively large cuticular scales, and are even regarded by some as identical, it seems better to retain the distinctive terms primary hair, in the restricted sense, as referring to the early hairs of the fetus, which perhaps under the stimulus of something derived from the maternal circulation, hypertrophy into lanugo, and secondary hair as referring to the fine hair of the postnatal

life. Convenience of usage, however, should not obscure the important fact that the morphologic type which characterizes the very first hairs of the fetus is still found virtually unchanged right through to the end of life.

The coarse, longer and more heavily pigmented hair which develops, especially at and following puberty, represents a third phase which most German and English speaking authors designate as terminal hair, in the sense that it is the presumed ultimate stage of hair development. Terminal hair characteristically has a well developed medulla through the greater part of its length and flattened or crenate cuticular scales. It ranges in character from the bristle to the awn. Hairs representing all stages of transition between bristles and the finest down may be found on any ordinary subject.

In his discussion of human pilosity, Friedenthal recognizes three stages in the development of the hairy covering. The first or "wool hair covering," that of the fetus, is characterized by the universally distributed primary hairs arranged in groups of from one to three, or rarely, five. The next, or "child hair covering," lasting until about puberty, consists for the most part of "wool" (secondary) hair arranged as before except that the coarse eyebrows and eyelashes are all placed singly. The hair of the head is coarser and shows a tendency toward the group arrangement. Finally, the "permanent hair covering" of the adult is characterized by the addition to the "child hair covering" of terminal hair which varies in amount according to the race, sex, and even the individual. The greater part of the body, at least in the female, is still covered by down.

ARRANGEMENT AND DIRECTION OF HAIR

The arrangement of hair is a matter of considerable interest. Its phylogenetic interpretations have already been mentioned. Friedenthal maintains that while the arrangement of down may be such as to suggest scales, the single hairs or groups of hairs being placed at the intersections of two imaginary sets of oblique parallel lines, the resemblance is after all only superficial, since the real explanation of the arrangement of the groups is to be found in the distribution of elastic tissue fibers in the corium. If this is correct, the similarity which Friedenthal has shown to exist between the arrangement of primary (and secondary) hair in man and the arrangement of hair in American monkeys presumably has its immediate cause in a similarity in the elastic tissue arrangement in these monkeys and young human beings. Terminal hairs in man occur singly at first but may subsequently appear in groups, and occasionally show a tendency to become arranged in rows. This point is stressed by Friedenthal, who regards it as significant from an evolu-

tionary standpoint that the young human being should have an arrangement of hair suggestive of the lower primates, while the adult has an arrangement more closely resembling that of the higher apes.

Another phase of hair arrangement which has attracted a good deal of attention is the matter of the direction of hair in different parts of the body—the hair streams or hair slopes. Since nearly all hair follicles have an oblique position in the skin, the tip of each hair points in a characteristic direction, which is obviously determined by the direction of the follicle from which it grows. What in turn determines the direction of the follicle is not answered so easily. The hair slopes in man

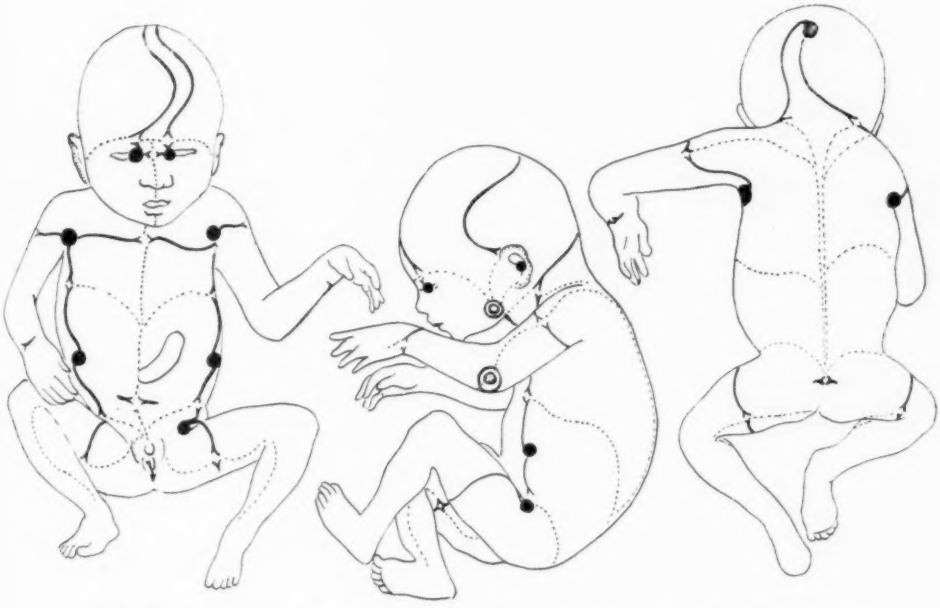

Fig. 34.—Diagrams show the direction of hair in a 7 months fetus (Friedenthal). Solid black lines represent divergence of hair streams, dotted lines convergence. Hair whorls are represented by solid black circles and "convergent whorls" or tufts on elbow and neck by concentric circles.

depart widely from those of the simpler forms where the majority of hairs point from before backward. Most of the early investigators worked on the fetus and young infant, but some studies, notably those of Kidd, have been based on the adult. A few slight changes take place between the two age periods.

Incidentally, there is also found more or less individual variation in the direction of hair. Several of the more constant phenomena of hair direction have been noted and are indicated in the illustrations (Figs. 34-37). All the hairs over a given surface usually point in essen-

tially the same direction. Such an area of parallel hairs is called a hair stream or hair slope. Two adjacent hair slopes may be at their common boundary either convergent or divergent, the former condition tending to produce a crest, the latter a natural parting or feathering. At the end of either of these lines, there is at least a potential whorl or cross (Fig. 35).

One of the earliest suggestions as to the cause of the hair slope is attributed by Eschricht to Osiander, who discussed the matter in 1816. Osiander seems to have believed that the direction of the hair follows the direction of the subjacent arteries. This was easily disproved as was

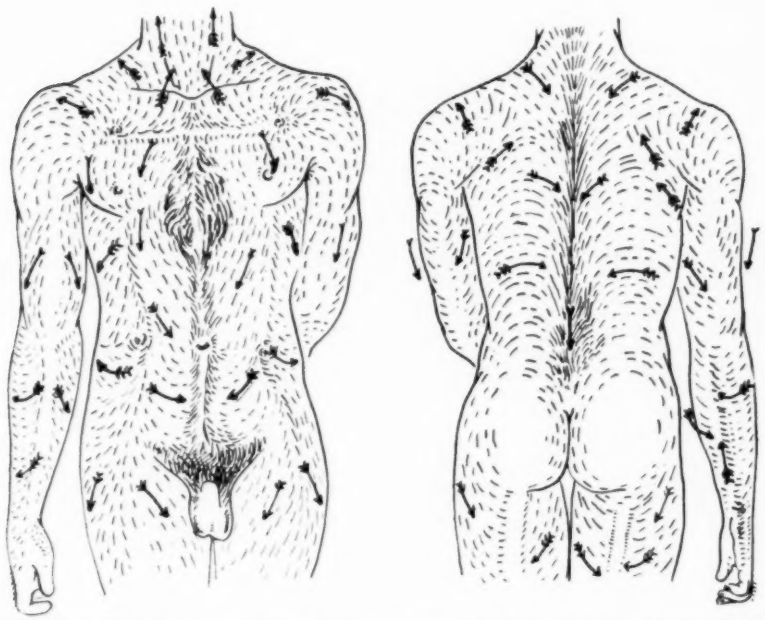

Fig. 35.—Direction of hair streams on the body and upper limbs (Kidd). Arrows with single barbs represent the presumed primitive arrangement; others show areas in which this arrangement has been modified.

also any suspicion of a definite association between hair direction and nerve distribution. According to Voigt (1856), the direction of hair is determined by the tension resulting from the unequal growth of different parts of the fetus, very much as the slope of a nutrient foramen is said to result from unequal growth of bone with reference to surrounding tissues. This theory has a certain degree of plausibility as applied to certain parts of the body and may be a factor of limited importance. According to Friendenthal and others, the direction of the follicle is determined by the tension of the elastic tissue elements in the skin. This suggestion probably comes nearest to offering a satisfactory mechanical

explanation but is not wholly adequate, since there is some lack of coincidence between direction of hair and elastic tissue pull. Schöne was unable to reverse the direction in the mouse by autoplastic transplants in which the skin flaps were turned end for end.

SUPPOSED ADAPTIVE CHANGES IN THE HAIR SLOPE

In this connection, the ingenious speculations of Kidd cannot be passed over. According to Kidd, the direction of hair is determined primarily by mechanical forces, which may be in the nature of external pressures and friction, and even gravity, or the internal pull of muscles and subcutaneous tissues. The arrangement of the hair may be modified during the life time of a person, in which case the modifications tend to be transmitted to the next generation. In his book on the subject, Kidd presents a considerable body of evidence in support of this kind of "use inheritance," but much of it is contradictory and on the whole

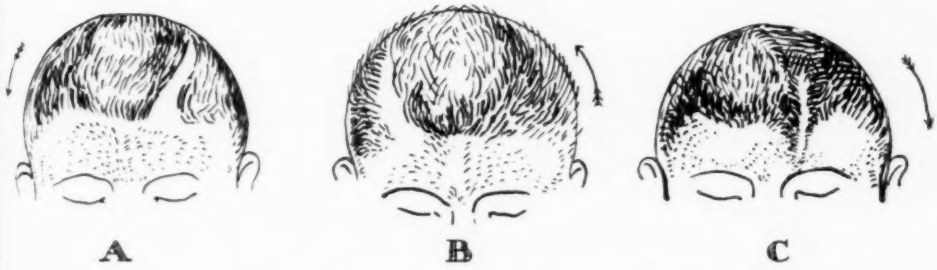

Fig. 36.—Three cases of natural parting in young subjects (after Kidd). *A*, the commonest arrangement with hair directed downward and parting to the left; *B*, parting to the right of the median line; *C*, parting to the left and continued down to the eyebrow.

unconvincing. For example, there is commonly a natural parting of the hair on the head (Fig. 35), and Kidd in examining seventy infants and young children found that forty-five of them showed a left lateral, seventeen a central, and six a right lateral parting. Two others had an unusual arrangement. These natural partings correspond in position and perhaps in frequency with the usual partings made in combing the hair, and lead to the inference that "probably most of them, certainly some, are produced in the individual by the inherited effects of dressing the hair in ancestors." The force of this and similar instances of the supposed inheritance of acquired modifications is considerably diminished by the equally striking cases which it seems impossible to explain in this way. For example, there is a frequent break in direction of the hair near the medial extremity of the eyebrow, attributed by Kidd himself to the effect of the subjacent corrugator muscle. The incidence of this

common condition was determined by Kidd from 200 consecutive cases, in which it was found that the break or parting was more marked on the right side in only fourteen instances. It was equally well marked on both sides in thirty-three subjects and more marked on the left in 153. In other words, despite the fact that it has never been the custom to part the eyebrows, there is as strong a tendency for the hair of the left eyebrow to show a natural part as for the hair on the left side of the scalp, and consequently the assumption seems justified that neither the one nor the other is due to any past ancestral custom, but that some other explanation must be sought for both. That the modes of hair dressing, on the other hand, have been influenced by the natural proclivities of the hair might be urged with some degree of plausibility. In passing, it may be noted that the natural parting of the hair in the eyebrow may represent a

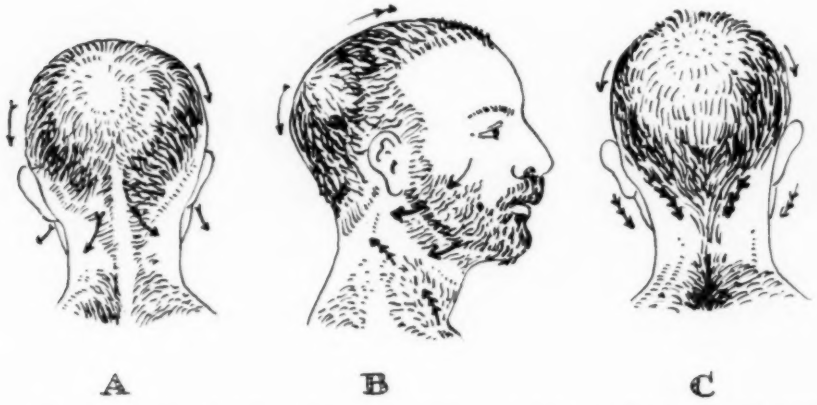

Fig. 37.—Three sketches showing direction of hair on the head and neck (after Kidd). *A* and *C* show two different natural arrangements in the back of the neck; *B* shows especially the reversed direction of hair in the anterior triangle.

continuation of the line of parting on the scalp. Kidd presents a figure (36 C) which strongly suggests such an interpretation, but he does not comment on this possibility. It would be of interest to determine the correlation between a left parting of the hair on the scalp and that of the left eyebrow.

One instance of the failure of the hair direction to become adapted to new conditions may be cited. The natural direction of hair in the submaxillary region is downward, while in the lower part of the neck it is upward, the two streams meeting in a line well within the beard covered area of most men (Fig. 37 B). Despite the frequent irritation that comes from shaving against the natural direction of the hair on the part of a considerable proportion of men for many generations, this peculiar

arrangement, apparently not shared by apes, still persists as a characteristic human trait.

On the ulnar side of the arms, the prevailing direction of the hair toward the elbow has frequently been emphasized, and since the time of Darwin and Wallace explained as an adaptation brought about through natural selection. This particular arrangement is presumed to have been acquired first in forms which during rain crouch with hands clasped back of the neck, the hairs of the arm and forearm forming a natural thatch which sheds the water freely from the slightly protruding elbows. In man, the arrangement is assumed to be a useless heritage from an apelike ancestor in which this habit was developed. The plausibility of this explanation is reduced by the fact that in the arm there is a fairly good agreement between the direction of hair and of cutaneous connective tissue bundles.

In spite of much unreliable and conflicting evidence, the possibility that the direction taken by hair on different parts of the body is such as to be more or less advantageous to the individual, cannot lightly be dismissed. According to Kidd, the hair arrangement in man deviates markedly in many particulars from that of any of the apes, and some explanation for the differences is needed. A satisfactory hypothesis will have to account for whatever differences may exist between the direction of hair follicles and lines of tension in the skin of the same region.

Abstracts from Current Literature

Observations After Ten Years on a Series of Cerebrospinal Syphilitics Treated by Intravenous and Intraspinous Therapy. George Draper, Am. J. M. Sc. **169**:39 (Jan.) 1925.

This is a report on a series of twenty-five cases treated in 1915 by the Swift-Ellis method, and a summary of twenty recent cases. According to the findings recorded at present in those treated ten years ago, Draper believes that the Swift-Ellis method is effective in a certain type of case, in his series representing 36 per cent. He also states that, in his opinion, successful results do not depend entirely on the use and action of arsphenamin and mercury, but depend partly on some resistance-raising factor produced during treatment without which antisyphilitic treatment will not check the progress of the disease. He advises all apparently cured persons to have a spinal fluid test at least every two years.

Syphilis of the Digestive Organs. W. E. Gatewood, Am. J. M. Sc. **169**: 253 (Feb.) 1925.

Of 12,000 patients admitted to the hospitals, only 0.37 per cent. were found with syphilis of the digestive organs, twenty-one showing clinical evidence of liver changes and only one in 470 cases of secondary syphilis giving any evidence of liver damage. Twenty patients had symptoms of cirrhosis or gumma or both. Syphilitic pancreatitis was found in two cases — clinically there was little relation between syphilis and diabetes — and only three cases of syphilis of the stomach and one case involving the large and small intestines were found.

Ringworm of the Toes as Found in University Students. S. H. Hulsey and F. M. Jordan, Am. J. M. Sc. **169**:267 (Feb.) 1925.

An examination of the toes of 100 students revealed 67 per cent. with a clinically positive ringworm; 49 per cent. were positive microscopically, while only 5 per cent. were culturally positive. Residence bore no relation to the incidence of the condition, nor was it confined to the dispensary type of patient. A small proportion (10 to 15 per cent.) had had ringworm previously.

The Incidence of Syphilis of the Aorta with Interstitial and Parenchymatous Neurosyphilis. J. H. Musser, Jr., and A. E. Bennett, Arch. Int. Med. **34**:833 (Dec.) 1924.

An analysis of the spinal fluid in thirty cases of syphilitic aortitis revealed an associated cerebrospinal involvement in 20 per cent. of the cases. Postmortem findings regarding this association of vascular and nervous system syphilis showed that 38 per cent. of the cases of vascular neurosyphilis had late syphilitic aortitis; of 110 cases of general paralysis, 28 per cent. had aortitis syphilitica; of fifty patients with tabes, 26 per cent. had syphilitic involvement of the aorta, aneurysms being more frequent in the vascular neurosyphilis type.

THE SKIN CAPILLARIES IN RAYNAUD'S DISEASE. G. E. BROWN, Arch. Int. Med. **35**:56 (Jan.) 1925.

The author reports on a study of eight cases of this disease with regard to the capillaries during different color phases.

JAMIESON, Detroit.

ACUTE DISSEMINATED LUPUS ERYTHEMATOSUS. REPORT OF THREE FATAL CASES. C. S. KEEFER and A. R. FELTY, Bull. Johns Hopkins Hosp. **35**:294 (Sept.) 1924.

Three cases of acute disseminated lupus erythematosus are reported. In two cases, the pathologic findings are described. The clinical features are almost similar in all three cases. Pathologically, the only constant feature common to both cases in which necropsy was performed was small groups of tuberculous lymph glands. No extensive tuberculous lesions were found. In one of the cases that came to necropsy, tubercle bacilli of the human type were recovered from a lymph gland which did not show the histologic lesion characteristic of tuberculosis.

In the third case there was a glandular enlargement. One gland excised while the patient was alive showed only lymphadenitis (toxic). Necropsy was refused. One of the cases that came to necropsy showed great increase in the size of the retroperitoneal, pelvic and inguinal glands. On section, most of the glands were tuberculous. Several such glands formed along the spinal column as high as the diaphragm.

At least two of these cases give evidence of the tuberculous origin of lupus erythematosus disseminatus.

McCAFFERTY, New York.

THE DIAGNOSIS OF CANCER. JAMES EWING, J. A. M. A. **84**:1 (Jan. 3) 1925.

Ewing states that the pathologist can render the most efficient service only if he is considered in the light of a consultant and given access to all the available information about any case in which he is consulted. He states that biopsies are at times indispensable aids, and seldom result in harm if the tumor is accessible and the growth not under great tension. For biopsy, Ewing prefers the knife to the cautery.

The pathologist should not be content with giving an histologic report alone, but should determine as far as possible the stage of the disease and the prognosis.

THE EXPERIMENTAL PATHOLOGY OF CANCER. F. C. WOOD, J. A. M. A. **84**:4 (Jan. 3) 1925.

The author discusses in a general way the important questions of cancer that have received some elucidation by laboratory methods, particularly those studies that have been made with transplantable tumors.

Though occasionally grafted tumors will regress spontaneously, no advance has been made in the study of this phenomenon. It has been observed that immunity to further transplants occurs after spontaneous regression of a tumor, but study of this has not lead to any serviceable results.

Wood studied the effect of biopsy on the metastasis of inoculated rat carcinoma and found it had no effect in inducing metastasis. He thinks that the danger of biopsy in man may have been overestimated.

In studying radiation dosage, it was found that the biologic sensitivity of the human skin and animal tumor were equal. No closure of the lymphatics following radiation could be demonstrated, nor could increased resistance of rat carcinoma to radiation be determined following sublethal tumor doses. This question, however, remains open for further investigation.

External Cancer. M. F. Engman, J. A. M. A. **84**:103 (Jan. 10) 1925.

The author believes that the classification of epithelioma into basal cell, squamous cell, nevocarcinoma and Paget's disease is a useful one, though tumors not characteristic of any type or of mixed type are occasionally encountered.

Probably one of the important factors in the determination of malignancy is a change in the environmental conditions of groups of cells.

The clinical features of the types of epithelioma are discussed and illustrated by photographs.

Treatment of General Paralysis by Inoculation with Malaria. H. A. Bunker, Jr., and G. H. Kirby, J. A. M. A. **84**:563 (Feb. 21) 1925.

The authors followed von Jauregg's method of malarial inoculation in the treatment of fifty-three patients with general paralysis. There was no selection of cases, except that moribund, far advanced, and emaciated patients were excluded. Tertian malaria was inoculated by the intravenous method; each patient was allowed from eight to ten febrile attacks, and arsphenamin was not administered subsequently. There were no serious complications.

For various reasons, fourteen patients were necessarily excluded from the appraisal of results, leaving thirty-nine cases for evaluation of the method. Of this number, five patients died during treatment, and one some months subsequently. Three of these patients died as a direct result of convulsions, which may be of significance in respect to treatment by inoculation malaria.

Of the thirty-two patients alive at the end of from three to thirteen months after treatment, fourteen show little or no improvement, while eighteen are much improved, with fairly complete remissions. Seventeen of these patients have been discharged, and fourteen have returned to their former occupations.

The influence of this treatment on the spinal fluid serology is not particularly evident, though there appears to be a slow but distinct improvement in some cases. Serologic improvement does not parallel clinical improvement regularly.

The authors conclude that the treatment of general paralysis by inoculation with tertian malaria is of indubitable value. This method definitely arrests the clinical progress of the disease in a considerably larger proportion of cases than would exhibit spontaneous remissions.

A Clinical and Experimental Investigation of Arsphenamin Poisoning. S. Weiss, J. A. M. A. **84**:577 (Feb. 21) 1925.

The author's experimental investigation was directed toward the production of acute yellow atrophy of the liver as the result of arsphenamin administration. The animals (cats) used in the experiments did not develop anything resembling acute yellow atrophy in man, the liver showing only minor pathologic changes even when previous chloroform administration had damaged the liver to a certain extent.

A study of the records of twenty-nine deaths due to arsphenamin in New York City showed that the drug probably plays an indirect but never a direct rôle in those cases of acute yellow atrophy occurring during arsphenamin treatment.

UNILATERAL HYPERHIDROSIS AND EROSION OF TEETH FOLLOWING PAROTID ABSCESS. W. T. VAUGHAN, J. A. M. A. **84**:583 (Feb. 21) 1925.

A case is reported of erosion of the teeth in both the upper and lower left jaw, associated with hyperhidrosis of the left side of the face. The patient previously had a left parotid abscess, and the cause of the erosion was apparently failure of the atrophied left parotid to neutralize the acid secretion formed in the gums. The association of hyperhidrosis of the face and parotid abscess is not unusual, but the associated dental erosion has not been recorded previously.

VALUE OF ELECTROTHERMIC METHODS IN THE TREATMENT OF MALIGNANCY. G. E. WARD, J. A. M. A. **84**:660 (Feb. 28) 1925.

The author takes up the technic of electrocoagulation and discusses its usefulness in various benign and malignant conditions. It is of value in superficial malignancies either alone or combined with radiotherapy or surgery. It adds a great deal to the other methods used in the successful treatment of cancer.

THE MENACE OF POORLY FITTED SPECTACLES IN OLD PERSONS. J. J. MORTON, J. A. M. A. **84**:666 (Feb. 28) 1925.

Four cases are recorded of epithelioma occurring as the result of prolonged irritation from improperly fitted spectacle frames. The points which require greatest attention are the bridge of the nose, the temples, and behind the ears.

HEMOCHROMATOSIS: REPORT AND DISCUSSION OF A CASE. STUART WILSON and F. A. WEISER, J. A. M. A. **84**:800 (March 4) 1925.

The authors report a case of this rare disorder having the characteristic features of diffuse pigmentation, enlarged liver, hemosiderin granules in the skin, hyperglycemia, and glycosuria.

The differential diagnosis from Addison's disease, cirrhosis of the liver, diabetes mellitus, arsenical poisoning, argyria, and visceral syphilis are discussed.

MICHAEL, Houston, Texas.

SKIN INFECTION OF RABBITS WITH HEMOLYTIC STREPTOCOCCI ISOLATED FROM A PATIENT WITH ERYSIPELAS. 1. METHOD OF DEMONSTRATING PROTECTIVE ACTION OF IMMUNE SERA. T. M. RIVERS, J. Exper. Med. **41**:179 (Feb.) 1925.

Phlegmonous and erysipelas-like lesions were produced in rabbits by intradermal injections of cultures of hemolytic streptococci of erysipelas. Repeated inoculations resulted in the production of a serum capable of preventing this injurious action, and it was found possible to test this serum for protective substances by injecting various dilutions of the serum and suspensions of streptococci in normal rabbits.

FURTHER OBSERVATIONS ON THE TREATMENT OF ORIENTAL SORE BY MEANS OF PHOSPHORUS. A. CASTELLANI, J. Trop. M. **27**:263 (Oct.) 1924.

The use of oleum phosphoratum, B. P., is recommended in oriental sore, applying the oil externally every other day after the removal of the crust if ulceration has occurred. If the lesion is nodular but not ulcerative, injections of the oil (3 to 5 minims) are made under and around the lesion once or twice a week. Three cases are reported in which the patient was cured by this method.

TINEA LABIALIS (BETEL-NUT DERMATITIS OF LIPS). W. R. MENDELSON, J. Trop. M. **27**:284 (Nov.) 1924.

Three betel-nut chewing Siamese women developed a peculiar itching dermatitis of the lips accompanied by slight redness, the areas involved soon becoming scaly and later depigmented. Cultures from the betel-nut cud and from the lesions showed an unidentified mold, and it was thought that a slight injury was the starting point of the infection. All were rapidly cured with a 3 to 5 per cent. salicylic acid ointment.

BRIEF NOTE ON A PERSISTENT CASE OF ORIENTAL SORE OF THE FACE, SUCCESSFULLY TREATED BY PHOSPHORATED OIL. H. V. KELAART, J. Trop. M. **27**: 288 (Nov.) 1924.

The ulcer in this case was situated on the face, was 7 by 3 cm. in size and had persisted for eighteen months in spite of vigorous tartar emetic and arsphenamin treatment. The lesion was healed in two weeks by local applications of phosphorated oil (Castellani's method).

NOTES ON PRURITUS ANI OF MYCOTIC ORIGIN. A. CASTELLANI, J. Trop. M. **27**:304 (Nov.) 1924.

In eleven of fifty-four cases of pruritus ani, fungi of epidermophyton and trichophyton groups were found in cultures, although in most cases there was no external evidence of mycotic infection. A few patients had had tinea cruris several years before. Pruritus was severe even in the absence of dermatitis or infection. Spontaneous cure was not observed, many cases, however, becoming dormant for variable periods of time. Deek's ointment gave good results in some cases.

	Parts
Salicylic acid	10
Subnitrate of bismuth	10
Mercuric salicylate	4
Eucalyptus oil	10
Petrolatum	..
Hydrous wool fat q. s. ad	100

Roentgen-ray treatment was often beneficial in chronic cases.

CUPRIC AND CYANOCUPRIC PREPARATIONS IN THE THERAPY OF TUBERCULOSIS AND LEPROSY. F. RHO, J. Trop. M. **27**:315 (Dec.) 1924.

In a series of ninety-eight cases, there were eleven cases of cutaneous tuberculosis with cures in all, six cases of lupus, four of which were cured, and three cases of lupus erythematosus, all cured. Ulcerated forms were treated with copper compounds.

In twenty cases of leprosy of different types, almost all cases were improved after approximately ten injections of a preparation containing potassium cuprocyanide, the author states that only a few refractory cases did not respond after twenty injections. Further courses of treatment were also necessary.

A New Type of Blastomycosis Cutis. A. Castellani, J. Trop. M. **27**:326 (Dec.) 1924.

A case is described in which there were pyogenic lesions on the scalp involving the follicles with the production of alopecia, some of which was permanent. Cultures yielded principally *Staphylococcus aureus* with an occasional yeastlike cell. This was later found to be a cryptococcus which was agglutinated by the patient's blood. The condition improved with cryptococcus vaccine and potassium iodid internally, while staphylococcus vaccine had no effect.

Granuloma Inguinale. A. R. Fraser, J. Urol. **13**:227 (Feb.) 1925.

A complete summary of the subject is given, with a report of eighteen cases of granuloma inguinale treated at Cape Town. Fraser is of the opinion that spontaneous recovery does not take place, and that many patients remain uncured even though every variety of medication be tried. He does not consider antimony a specific for the condition as it is seen in South Africa.

Jamieson, Detroit.

Intradermal Injections of Foreign Proteins in the Treatment of Cutaneous and Venereal Diseases. C. Convert, Riforma med. **41**:55 (Jan.) 1925.

The author has used intradermal injections of milk and modified milk in the treatment of eighty-six patients with venereal bubo, impetigo, furunculosis, sycosis, vulgaris, acne, eczema and gonorrheal complications. In impetigo, furunculosis, pyoderma and acute eczema, the results were encouraging.

Serotherapy of Syphilis. F. Jauregui and L. Lacelotti, Rev. méd. Latin Am. **10**:313 (Dec.) 1924.

The authors have been able to transmit human syphilis to the South American llamas and have maintained infected animals for the last nine years. The disease confers immunity to the animals. The serum of immunized llamas has been used for the treatment in fifty cases of human syphilis. The results obtained in these cases are as follows: The period of chancre is shortened, the lesions of the secondary type are greatly attenuated, and the serologic reactions become negative. Several of these patients who have been followed for the past three years have presented no further manifestations of the disease, and their serologic reactions remain negative. The authors are conservative in their conclusions, stating that they claim only to have initiated a new chapter in the field of experimental syphilis which is open to investigation and criticism.

Cubitus Valgus, a Stigma of Heredosyphilis. P. L. Baliña, Rev. dermat. Argentina **10**:45, 1923.

Report of a case of this bone deformity in a man aged 41, with numerous stigmas of hereditary syphilis. The author calls attention to the frequency of cubitus valgus in cases of hereditary syphilis.

EUCHININ IN THE TREATMENT OF PRURIGO. P. L. BALIÑA, Rev. dermat. Argentina **10**:57, 1923.

Baliña recommends the administration of this quinin salt in doses of 5 cg. per year of age, daily by mouth. The course of treatment lasts ten days, followed by a rest of ten days and a new course if necessary. Very good results are reported.

ENDOCRINOUS DISTURBANCES IN ECZEMA. J. L. CARRERAS, Rev. dermat. Argentina **10**:103, 1923.

The author has found symptoms of endocrinous disturbance in 250 of 430 cases of eczema examined. Epinephrin, thyroid and in some cases pluriglandular extracts proved curative.

PARDO-CASTELLO, Havana.

DERMATOLOGIC ABSTRACTS

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

PERNICIOUS ANEMIA IN ITS RELATION TO SPRUE. E. J. WOOD, Am. J. M. Sc. **169**:28 (Jan.) 1925.

Wood asserts that as readily in pernicious anemia as in sprue, *Monilia psilosis* can be recovered from the feces, the gastric contents and the gums, when pyorrhea exists. By feeding guinea-pigs with *Monilia psilosis*, a hemolytic anemia was produced. There were also produced changes in the liver and bone marrow which were suggestive of the action of a hemolytic poison. A filtrate of *Monilia psilosis* in dextrose water, injected intravenously into rabbits, caused blood changes apparently hemolytic in nature.

SURGICAL TREATMENT OF ROENTGEN-RAY LESIONS. C. A. PORTER, Am. J. Roentgenol & Radium Therapy **13**:31 (Jan.) 1925.

Porter says that in ordinary malignant disease, to get rid of both the local lesion and the glands will cure the disease; but in these roentgen-ray cases the guardian glands should be preserved as long as possible for they are very often simply enlarged from adenitis and to a certain extent prevent the metastasis of cells to the rest of the body.

LUPUS IN ITS SURGICAL ASPECTS. W. S. HANDLEY, Ann. Surg. **81**:9 (Jan.) 1925.

Handley asserts that lupus is not a skin disease. It is a disease of the lymphatic system not restricted to the skin, and governed as to its mode of spread by the facts of lymphatic anatomy. Tuberculous lupus presents all the marks of a disease spreading by continuity in the lymphatic vessels. It is in fact essentially and primarily a disease of the lymphatics, a destructive lymphangitis of the parietal lymphatic system. The treatment employed by Handley is based on this pathologic conception.

PELVIC ACTINOMYCOSIS. W. M. BRICKNER, Ann. Surg. **81**:343 (Jan.) 1925.

Brickner describes the surgical treatment, with recovery, of five consecutive cases of pelvic actinomycosis in which the disease lasted three, eleven, four, two, and twenty years, respectively. In one case the pelvic involvement was a late extension. In one case there were four outbreaks circumscribed to the groin with latent intervals of six to seven years.

TRYPARSAMIDE IN SYPHILIS OF THE NERVOUS SYSTEM. S. I. SCHWAB and L. D. CADY, Arch. Neurol. & Psychiat. **13**:80 (Jan.) 1925.

The experience of Schwab and Cady seems to indicate that tryparsamide in the treatment of neurosyphilis combined with arsphenamin and some of its derivatives and mercury offers, for the present at least, a more hopeful outlook for these cases than any other drug or combination of drugs that has been tried. It presents a more advanced type of treatment than intraspinal medication or the use of any other method.

RESULTS OF ADMINISTRATION OF TRYPARSAMIDE IN SYPHILITIC DISEASE OF THE NERVOUS SYSTEM AND IN CERTAIN OTHER DISEASES OF NEUROSYPHILITIC CHARACTER. F. KENNEDY and T. K. DAVIS, Arch. Neurol. & Psychiat. **13**:86 (Jan.) 1925.

Kennedy and Davis are of the opinion that, in general, the benefits from the drug exceed the untoward effects, since it appears possible and easy to prevent optic nerve changes that are organically permanent, by proper control of dosage. Three grams of the drug is a maximum dose, in their opinion, and they believe that it would be better to have 2 gm. established as the average full-sized dose rather than 3 gm. Injections should be given at intervals of at least seven days. Leakage into the tissues does not cause cellulitis. It is practical to give injections in series of eight consecutive weekly treatments followed by a brief rest period of two weeks. However, there is no definite contraindication to having the second series immediately follow the first. Two or even three series are warranted in cases displaying beneficial results. Improvement, if it occurs at all, almost always occurs early. Mercury should be used in conjunction with tryparsamide. Unconditional marketing of the drug seems justifiable if explicit directions regarding dosage and intervals are clearly stated on every bottle, and if the dangerous possibilities are sufficiently explained. The drug should not be used on patients when ophthalmoscopic examinations cannot be carried out regularly.

RESULTS OBTAINED WITH TRYPARSAMIDE IN GROUP OF FIFTY CASES OF NEUROSYPHILIS. C. S. BLEUMEL and W. M. GREIG, Colorado Med. **22**:16 (Jan.) 1925.

Fifty patients with general paralysis, tabes and other forms of neurosyphilis were given sixteen injections of tryparsamide at weekly intervals by Bleumel and Greig. Sixteen patients improved; sixteen showed no material change; nine were worse, and nine died during treatment. Four suffered visual impairment amounting virtually to blindness.

MODERN CONCEPTION OF SPIROCHETOSIS. A. PHILIBERT, Medicine **6**:207 (Dec.) 1924.

Philibert reviews the spirochetal infections that have been listed in the last twenty years; up till then only relapsing fever had been definitely recog-

nized as a spirochetosis. All seem to be obligatory septicemias and this entails vascular lesions as a common feature. The liver and kidneys are always more or less affected, and also the meninges and nerves. Spirochetoses are distinguished further by their cyclic course, and in the acute forms this corresponds to a cyclic evolution of the parasite. In the latent periods, although the spirochete cannot be detected in the blood, it must be present in some other form, as the blood remains virulent. Another common feature is the obligatory contagiousness; direct in syphilis and yaws, only by an intermediate host in the majority of spirochetoses, but all the tissues seem receptive. Other common features are that the disease does not confer immunity, and that the Wassermann reaction is positive in all during the acute phase. Typhus, multiple sclerosis and other diseases may prove of spirochetal nature, which would give hope of successful treatment, as we have powerful weapons already against the spirochetoses.

Case of Orbital Hemangioma Treated with Radium. A. C. Jones, Northwest Med. **24**:11 (Jan.) 1925.

Jones reports a case of cavernous hemangioma of the orbit, not involving adjacent structures, which was successfully treated with radium. The patient was 6 years of age. He was first seen in May, 1923. Since then there has been a steady improvement in the vision and recession of the tumor, until now it is impossible to detect any difference of the two eyes and appendages. There is binocular vision. This is said to be the first case of cavernous hemangioma of the orbit treated with radium.

Absence of Arsphenamin Reactions in Syphilis. M. Haase and C. H. Marshall, Southern M. J. **17**:837 (Nov.) 1924.

During three years and eight and one-half months, 17,877 injections of the old arsphenamin have been given in the syphilic clinic at the Memphis General Hospital. Of this number, 3,029 have been given to white patients and the remainder to colored. Haase and Marshall assert that from these injections there has not occurred a single severe reaction; that is, no case of exfoliative dermatitis, severe jaundice, severe kidney damage or of encephalitis. Of the mild reactions occurring at the time or soon after the injection, there have been seventeen. These included the "nitritoid" crises occurring at the time of injection, nausea, vomiting, and rise in temperature occurring from a few minutes to a few hours after the dose was given. No cutaneous reactions were observed.

Effect of Surgical Trauma, in Patients with Syphilis; Healing of Postoperative Wound. W. H. Goeckerman, Surg., Gynec. & Obst. **60**:77 (Jan.) 1925.

A review of the cases of fifty patients with syphilis who have been subjected to various surgical procedures has convinced Goeckerman that these patients can be operated on with impunity. The patient whose infection is of long duration is on the whole a poor surgical risk, but only in proportion to the damage his tissues have sustained. He is no worse risk than another patient with an equal amount of damage from some other cause. Untreated patients rarely develop postoperative difficulties (7 per cent.), but operation on a gumma will increase the damage, and reflects on the diagnostic ability of the physician. In a suspected case, conservatism indicates careful treatment before

surgery is undertaken, if the lesion is not of an emergent character. The age, sex and anatomic systems involved seem not to influence the postoperative course. A considerable number of patients with syphilis are evidently operated on regularly without the surgeon being aware of the condition. A routine Wassermann test materially reduces this number. A dose or two of arsphenamin, preparatory to operation, is not necessarily a wise procedure, except as a protective measure for the surgeon.

REACTION OF SKIN TO VACCINIA VIRUS. J. C. G. LEDINGHAM, Brit. J. Exper. Path. **5**:332 (Dec.) 1924.

The vaccinal lesion has been studied histologically by Ledingham in its various manifestations following cutaneous, intraderma, subcutaneous, intravenous, intraperitoneal and intrasplenic inoculation, and both naked-eye and histological data have been controlled by inoculations of virus mixed with viricidal serum. The lesion is essentially of the order of an acute infective granuloma in which the reticulo-endothelial system is primarily and dominantly involved. There is no evidence that vaccinial virus possesses an elective affinity for epiblastic tissue. The lesions of vaccinia and of molluscum in the hen are histologically of the same order in so far as the dermal response is concerned. Evidence is afforded that precisely similar tissue responses occur when the virus is introduced into tissues remote from epiblast, such as the subcutis, the peritoneum and the spleen. In contradistinction to vaccinia, anti-epidermal serum when introduced intradermally produced an early and definite toxic action on epiblastic elements of skin.

NEW OUTLOOK ON CANCER: IRRITATION AND INFECTION. J. YOUNG, Brit. M. J. **1**:60 (Jan. 10) 1925.

An organism with a complex life story has been obtained almost constantly by Young from cancer. It possesses yeast, coccal, bacillary and amorphous phases, and each of these can grow true to type and live a wholly independent life. The parasite lives in symbiosis with the cancer cell in the amorphous phase, and it is from this that all the other phases are derived during incubation of a cancerous growth. The discovery of this phase, it is asserted, provides the key to the cancer phenomena, as also the key to the morphologic variants. The morphologic features of this parasite resemble the life story described by many writers for other classes of pathogenic organisms. The parasite belongs to familiar bacteria that are widespread in nature; and the ease with which cancer can be induced experimentally in animals by chronic irritation suggests that tissue susceptibility, wherever found, implies the immediate risk of infection by a ubiquitous organism. The free and universal exposure of man and animals to infection, combined with the (relatively) small proportion of the total that develop cancer, Young takes it, suggests the all-importance of cell susceptibility, and corresponds to the laboratory difficulties attendant on an attempt to produce cancer experimentally by the injection of the organism.

PROTEIN POISON THEORY. APPLICATION TO HEADACHE AND MIGRAINE. R. CURTIS-BROWN, Brit. M. J. **1**:155 (Jan. 24) 1925.

Curtis-Brown's theory differs from that of anaphylaxis, which has been generally accepted to explain various food idiosyncrasies. In anaphylaxis a preliminary sensitization is required, while Curtis-Brown maintains that the

metabolism of the individual is inadequate. Such an inadequacy for the metabolism of nitrogenous food is most usually inherited, but further damage can be prevented by appropriate diet. The protein poison may act directly on the tissue cells of the mucous membrane or the skin, causing, for example, in one instance bronchitis or colitis, and in another instance such a disease as eczema. Or, again, it may act indirectly, as through the endocrine or nervous system. Migraine occurs in persons who have inherited a damaged metabolism for nitrogenous foods. Headache is one of the commonest manifestations of protein poison. The headaches caused by protein poison vary in severity from the mildest headache to the severest forms of typical migraine. The etiology of all functional headaches is the same. In migraine, however, there is the typical inherited insufficient protein metabolism. Curtis-Brown says that the quickest and best way to ascertain what foods are deleterious in each individual case is to begin with a diet free from protein, especially animal protein, and then to build up gradually a suitable diet. The foods that he has found potent in causing headache are meat, fish, poultry, game and extract, such as soups and gravies made from them; eggs, milk and cheese; fruit and fruit juices; coffee, tea, chocolate and alcohol; and, among the vegetables, tomatoes and mushrooms. Curtis-Brown prescribes a diet of polished rice, butter, toast, a few green vegetables, and water. So soon as the headache is distinctly improved, the diet should be amplified, at first with other vegetables, then by a small amount of meat, once a day. Every article of nitrogenous nature must be suspected until proved to be harmless in the case under treatment. The protein of cereals and vegetables is usually well borne.

ACUTE BISMUTH POISONING. X. VILANOVA, Ann. d. mal. ven. **20**:25 (Jan.) 1925.

Vilanova describes a case of idiosyncrasy to bismuth in a syphilitic woman, under mixed neo-arsphenamin and bismuth treatment. The small total of 0.237 gm. of metallic bismuth in eighteen days induced phenomena of severe poisoning, characterized by grave lesions in the intestines, tubular nephritis, fever and stomatitis, similar to that from mercury. The nervous system was apparently not affected. The toxic symptoms persisted for a month; there had been no warning line on the gums.

MYOPIA FROM NEO-ARSPHENAMIN. MILIAN, Bull. et mém. Soc. méd. d. hôp. de Paris **48**:1765 (Dec. 6) 1924.

Milian reports two cases of syphilis in which every injection of neo-arsphenamin caused a transient myopia. The phenomenon appeared ten and thirty-eight hours after the injection, and persisted two days. It coexisted with a slight or pronounced albuminuria, and was preceded by general signs of intolerance. The myopia may be due to toxic paralysis of the sympathetic. He has noted this complication only four times within fourteen years.

ACTION OF RADIUM ON MICROBES. R. BRUYNOGHE and W. MUND, Compt. rend. Soc. de biol. **92**:211 (Jan. 30) 1925.

Bruynoghe and Mund assert that radium emanations inhibit in microbes the ability for division, without disturbing other vital phenomena, such as motility. Alpha and beta radiations exert also a direct action on trypanosomas in vitro, inducing lesions in the apparatus controlling cell division.

TREATMENT IN NEUROSYPHILIS. H. MARINESCO and S. DRAGANESCO, Presse méd. **33**:130 (Jan. 28) 1925.

On the basis of Hoff's experiments on animals with arsenic, and their own with trypan blue, Marinesco and Draganesco affirm that drugs administered intravenously do not reach the central nervous system. Only repeated intravenous injections, combined with subarachnoid injections, have a chance for success in treatment of neurosyphilitic affections. They used Gennerich's method in eighty-five patients with neurosyphilis. They drew from 50 to 120 c.c. of the cerebrospinal fluid, mixed with two thirds of the amount 1-1.8 mg. of neo-arsphenamin, and reinjected it. An intravenous injection of neo-arsphenamin followed the next day. Eleven patients out of seventeen with general paralysis improved; two presented a short remission after a grave recurrence; in four the treatment did not display any effect. In one of two with tabes and paralysis, an amelioration of clinical phenomena and changes in the reactions were manifest. Improvement in the ataxia and relief from pains were noted in five tabetics after four or five injections; also improvement of recent visual disturbances in one tabetic. Administration of 6-22 mg. of neo-arsphenamin, in four to seven subarachnoid injections, induced an improvement in seven cases of cerebral syphilis, submitted besides to a general treatment. It is emphasized that the results were superior to those from general treatment, and even from arsphenaminized serum in vivo.

CONGENITAL EDEMA. GOORMAGHTIGH and VAN CAUWENBERGHE, Bruxelles med. **5**:412 (Jan. 18) 1925.

Necropsy showed changes in the blood-producing and other organs analogous to those of leukemia, except that the excessive production was of erythrocytes. Goormaghtigh and Cauwenberghe ascribe the anomaly to tuberculosis in the parents.

HERPES ZOSTER AND CHICKENPOX. G. BATTINO, Pediatria **33**:31 (Jan. 1) 1925.

Battino concludes that the virus of chickenpox and of herpes zoster is identical or quite similar.

INTRADERMAL PROTEIN THERAPY. C. COUVERT, Riforma med. **41**:55 (Jan. 19) 1925.

Couvert injected milk and other proteins intradermally in various diseases. He confirms the good results in epididymitis. The effect was inconstant in eczema. Pyodermic affections gave fine results.

PANCREAS TREATMENT OF ECZEMA AND SEBORRHEA IN INFANTS. RUEDA, Semana med. **2**:1190 (Nov. 20) 1924.

Analysis of such cases seems to show that the assimilation of fat is not quite normal, and Rueda declares that it is logical to seek to reenforce the pancreas in its task of coping with the fat in the milk by supplying a homologous substance. He has been amazed at the success of feeding pancreas to such infants, and here reports a new series of cases, bringing the total to seventy-five in which seborrheic eczema of the scalp or elsewhere, and certain other forms of eczema, were effectually combated by feeding pancreas tissue

in tablet or pulverized form, from 0.5 to 2 or 3 gm. daily. The cure was complete in from one to four weeks. His series includes several cases reported by other physicians in Argentina and elsewhere.

EXPERIMENTS ON HERPES. E. GILDEMEISTER and K. HERZBERG, Deutsch. med. Wchnschr. **51**:97 (Jan. 16) 1925.

Gildemeister and Herzberg produced characteristic pustules in the heel of guinea-pigs by inoculation with the contents of vesicles from febrile herpes. Later passages of an originally weak virus may produce encephalitis in rabbits.

HAIR FASHIONS AND ECZEMA OF THE EAR. E. DOCTOR, Deutsch. med. Wchnschr. **51**:112 (Jan. 16) 1925.

Doctor incriminates the wearing the hair over the ears for the localization of eczema behind the ears. The perspiration cannot evaporate, and it macerates the skin.

EPIDEMIOLOGY OF SMALLPOX. O. CHEREFEDDIN, Deutsch. med. Wchnschr. **51**:114 (Jan. 16) 1925.

Cherefeddin's chart shows a four or five year periodicity of the small epidemics of smallpox in Constantinople. The residents in the city are well vaccinated, but safe protection seems to last only that long. The disease is always imported.

TEETH IN CONGENITAL SYPHILIS. E. LANGER and M. WASSMUND, Klin. Wchnschr. **4**:110 (Jan. 15) 1925.

Langer and Wassmund conclude from their observations that the cause of Hutchinson's teeth is in a syphilitic affection of the intermaxillary bone and the junction of the jaws. This accounts best for their localization near the middle line.

TREATMENT OF GENERAL PARALYSIS. A. KUTZINSKI, Med. klin. **21**:46 (Jan. 11) 1925.

Kutzinski treated a general paralysis patient with arsphenamin. Urticaria and prolonged fever followed. The patient recovered in every respect except for the changes of the pupils. Another patient, with absolutely typical clinical features of paralysis, gave entirely negative serologic and cytologic findings in the serum and cerebrospinal fluid.

EXPERIMENTAL CANCER RESEARCH. G. DÖDERLEIN, Monatschr. f. Geburtsh. u. Gynäk. **68**:139 (Jan.) 1925.

Döderlein insists that irreversible growth and autodestructive boring into the depths are the two characteristic features of experimental cancer. Metastasis and transplantability are not indispensable for the assumption of malignant disease, as we know that human cancer is not always accompanied by metastasis, while we see the animal die of the malignant disease even when transplants from it fail to "take." Experimental cancers have taught us that malignancy may be installed long before any histologic evidence of it is attainable. He regards it as significant that of all the numerous substances used to induce experimental cancer, only those succeed which are soluble in oil. The main thing in cancer research now is to learn why certain animals in the same litter develop cancer while others do not. What is the difference which

allows malignant growth in one and not in the other? Another promising field is the study of the histologic changes just preceding the development of cancer. When it induces visible changes, it is already far advanced.

VARIOLOID ERUPTION IN TYPHOID. C. GOTTSCHALK, München. med. Wchnschr. **72**:17 (Jan. 2) 1925.

Gottschalk observed an eruption resembling smallpox on the sixth day of typhoid in a lactating woman. Only staphylococci grew from the pustules. The patient recovered.

SKIN TESTS IN EXTENSIVE LICHEN. E. F. MÜLLER, München. med. Wchnschr. **72**:125 (Jan. 23) 1925.

Müller found no leukopenia after intracutaneous injections in a skin affected with extensive lichen. He believes that the centripetal pathways of the reflex were interrupted.

TREATMENT OF ARSPHENAMIN INFILTRATES. F. DIETEL, München. med. Wchnschr. **72**:128 (Jan. 23) 1925.

In the not infrequent mishaps in injecting arsphenamin into the tissues, Dietel aspirates as much of the injected arsphenamin as possible, and immediately injects a large amount of physiologic sodium chlorid solution in and around the infiltrate.

CHANGES IN THE CLINICAL PICTURE AND TREATMENT OF SYPHILIS. E. FINGER, Wien. klin. Wchnschr. **38**:27 (Jan. 2) 1925.

Finger agrees with Proksch's opinion that syphilis was not imported from America. It was classed in ancient times with lepra. The sixteenth century brought only a better diagnosis. It is natural that the grave cases predominate in the clinical descriptions. It is probable that the majority of patients had the same symptoms as we still find in neglected populations. He asserts, however, that syphilis has taken different aspects in the civilized countries in our times. Since the chronic treatment was instituted, it has ceased to be an affection of the skin and attacks chiefly internal organs — especially the central nervous system and the aorta, perhaps because the immunizing action of the skin cannot develop. Little of the specific remedies is necessary if the reaction of the organism is good. They are most valuable in the group which needs such a stimulation, and useless if the organism is unable to react. General roborant treatment is important. Besides this, the nonspecific remedies begin to play a great rôle. Kyrle has treated in Finger's clinic several hundred patients exclusively with arsphenamin and malaria inoculation. The results of one course of this treatment are very promising.

PATHOLOGY OF HERPES. LUGER and LAUDA, Wien. klin. Wchnschr. **38**:33 (Jan. 2) 1925.

Luger and Lauda review the pathology of febrile herpes and zoster and their relation to encephalitis. They believe in the multiplicity of etiology of zoster — especially because of the occurrence of varicella zosters. Lauda and Silberstein could not confirm the serologic identity of varicella and zoster.

ACTINOMYCOSIS OF FEMALE GENITALS. S. MITRA, Ztschr. f. Geburtsh. u. Gynäk. **88**:249 (Dec. 18) 1924.

In a case described, the vaginal portion of the uterus was the seat of the lesion. Necropsy confirmed that it was probably a primary process.

RELATION OF THE SYMPATHETIC SYSTEM TO DERMATOSES. J. GOLAY, Rev. med. de la Suisse Rom., Geneve **45**:39 (Jan. 25) 1925.

Golay illustrates this connection by the case of a woman, aged 25, with dermatitis herpetiformis, of a year's duration, and further manifestations, which he cites in proof of the origin of the skin disease in disturbances of the sympathetic system. They are: (1) the preeruptive nature of the accompanying pruritus; (2) the extraordinarily symmetrical distribution of the lesions; (3) the hyperhidrosis, and (4) the acute exacerbation at each menstrual period. The final proof, he says, was the improvement of the condition by desensitization with own blood and later with protein therapy. Protein therapy, according to Rosenthal and Holzer, owes its action to a modification of the excitability of the sympathetic system.

SMALLPOX AND CHICKENPOX. H. SAHLI, Schweiz. med. Wchnschr. **55**:1 (Jan. 1) 1925.

Sahli finds that all the diagnostic aids in differentiating smallpox from chickenpox in doubtful cases are unreliable. This applies to Paul's test on the rabbit cornea as well as to diagnostic vaccination. The latter may be positive in smallpox and negative in chickenpox. He promulgates a neo-unitarian theory: The virus of chickenpox is a mutation of the smallpox virus, a little farther removed than vaccinia. The difference in virulence is not merely quantitative, but qualitative. He believes that true smallpox may originate exceptionally from chickenpox.

PROTOPATHIC SENSIBILITY OF THE SKIN. BOEKE and HERINGA, Nederlandsch Tijdschr. v. Geneesk. **1**:4 (Jan. 3) 1925.

Boeke and Heringa report findings which conflict with Head's theory of protopathic sensibility. Their research was conducted on Heringa's hand which had been paralyzed after a fall in which the ulnar nerve had been severed by a broken pane of glass. The nerve was sutured an hour later, and the sensibility and histologic findings in an excised scrap of skin were studied during the following months as regeneration of nerve function proceeded.

INCUBATOR TREATMENT OF LEG ULCER. G. A. M. VAN BALEN, Nederlandsch Tijdschr. v. Geneesk. **1**:20 (Jan. 3) 1925.

As a last resort in a case of leg ulcer of three years' standing, in a woman of 62, bedridden from the cachexia and threatened gangrene of the foot, van Balen applied a hot air box to the leg, for three to six hours a day (39 C.). The relief of pain was prompt and in twelve weeks healing was complete. In the majority of his other cases, the cure was complete in three weeks. The leg is exposed bare in the oven, and outside only a protecting bandage is worn.

Society Transactions

MANHATTAN DERMATOLOGICAL SOCIETY

Cases Abstracted from Regular Meetings of 1923 and 1924

OSCAR L. LEVIN, M.D., *Chairman*

PAPULAR SYPHILODERM. Presented by DR. ROSEN.

A woman, colored, aged 24, with a generalized papular syphilitic eruption, was admitted to the Vanderbilt Clinic, Sept. 14, 1923. Associated with this syphilitic infection, the patient had an active gonorrhea. The patient was given arsphenamin intravenously and injections of mercuric salicylate intramuscularly. After the sixth intravenous injection, she developed a generalized erythema. There were also slight constitutional symptoms, fever, headache and malaise.

Examination revealed a generalized involvement with areas of redness and an intense pigmentation of the skin in the spots that the syphilitic papular eruption involved, and a depigmented ring around each of the pigmented lesions.

DISCUSSION

All agreed with the diagnosis as presented.

MULTIPLE BENIGN CYSTIC EPITHELIOMA. Presented by DR. GILMOUR.

C. L., a woman, aged 27, married, born in this country, had tumors on the face. Her mother, aged 63, for ten or twelve years had had a few similar spots on the face. Dr. Gilmour saw a sister, aged 24,, who had spots like the smaller ones presented by the patient. These had been present on the upper lip for one and a half years. A brother, aged 34, had a few spots. The father and a sister and three other brothers were free from the condition. The personal history was negative.

Eight years before presentation, a few hard, small, shotlike swellings had appeared on the forehead and nose. These had gradually increased to the present size. No symptoms were present, only disfigurement. Physical examination revealed many small, shot-sized, shiny tumors on the forehead and on the temples, about the color of the normal skin. Those on the forehead were discrete. On the bridge and on the right side of the nose in the right nasolabial fold and just above the right side of the upper lip, the growths were larger. Some were the size of small peas. In this location, especially in the right nasolabial fold, they were closely packed. Some appeared almost translucent. A few were slightly reddened, but not inflammatory. Some of the larger lesions had small blood vessels running over the surface.

DISCUSSION

All agreed with the diagnosis.

PSORIASIS WITH TUMOR FORMATIONS. Presented by DR. O. L. LEVIN.

L. G., aged 21, was first treated six years before presentation for universal psoriasis at the Mt. Sinai Hospital. Following local treatment with 3 per cent.

chrysarobin ointment and autoserum injections, the skin eruption disappeared. Six months prior to presentation, she appeared at the Cornell Clinic, showing a generalized, almost universal, psoriatic eruptions, with interesting lesions on both legs and thighs. On the front of the thighs, there were large, infiltrated, firm plaques, which were limited above by the psoriasis and below ran down to the tumor areas. On the front and backs of the legs, there were numerous round, irregular, elevated, firm and hard tumors, covered by thick scales varying in size from that of a pea to that of a small egg. The surfaces of some of these were rough and in places suggested rupial lesions. The first impression was that the psoriasis presented a premycosis fungoides, while the lesions on the lower extremities were those of a frank tumor stage of mycosis fungoides. Biopsy of the skin from lesions on the trunk as well as from the tumors presented a similar picture to that found in psoriasis. There was no microscopic evidence of mycosis fungoides. Subsequent to presentation, lesions were also removed from the leg and further examinations made. Pathologically, they presented psoriasis.

DISCUSSION

Dr. Howard Fox said that the tumor-like lesions on the leg might be considered as an unusual manifestation of psoriasis, one that he had not previously seen. A lichen planus hypertrophicus had been ruled out histologically. In reply to Dr. Rosen, he recalled a case of psoriasis of long standing which had been reported, on which mycosis fungoides had eventually developed.

Dr. Bechet could not suggest any positive diagnosis so far as the lesions on the leg were concerned, but he said that he did not believe they were psoriatic. They were distinctly tumor-like and nodular. Leukemia presented such varied cutaneous manifestations that he would like to inquire of Dr. Levin whether a blood count had been made.

Dr. Oulmann considered these granulomatous tumors on the legs as being due to continuous scratching, prurigo nodularis.

Dr. Levin said that when the patient first presented herself at Cornell, he considered the whole condition as mycosis fungoides. However, in view of the microscopic findings, the absolute lack of response to involution of the lesions with roentgen-ray treatment and absence of itching made him believe that this was a frank case of psoriasis with tumor formation. In discussing the effect of the roentgen rays in psoriasis, he stated that some cases of psoriasis responded well to the roentgen-ray; yet there were certain cases which did not respond, and other cases after clearing up would recur and prove more obstinate to roentgen-ray therapy. He also had noticed that in several cases in which the roentgen rays were used in psoriasis this form of therapy was followed by undue itching and the development of a generalized eczematoid eruption resembling pityriasis rosea.

Dr. Satenstein stated that the marked thickening of the epidermis was similar to that found in warts. He suggested giving roentgen-ray exposures of heavy intensity.

A Case for Diagnosis. Presented by Dr. Parounagian.

Mrs. M. B., aged 51, American, admitted to the Bellevue Clinic, July 2, 1920, at that time had an eruption and also a four plus Wassermann reaction. At this time, she received active antisyphilitic treatment although a definite diagnosis was not made. Since that time she had received further treatment, with

practically no change, either clinically or serologically. She stated that up to about one week before, the lesions had been much paler, but they had become more aggravated since. Distribution was symmetrical, involving both upper and lower extremities. The lesions were dark red, and the majority of them were circinate. The patient did not complain of subjective symptoms. Some time ago, a biopsy was made, which did not help in the diagnosis.

DISCUSSION

DR. WISE said that he thought this was Majocchi's disease, and referred to an article by Truffi, the illustration of which corresponded to the eruption on this woman — annular purpuric lesions, but no telangiectases. He thought there was enough clinical evidence to justify that diagnosis in this case.

DR. BECHET agreed with Dr. Wise. The lesions in Dr. Parounagian's case certainly resembled those of Majocchi's disease.

DR. SATENSTEIN said that three findings were missing which make this case fit in with Majocchi's disease — pigmentation, discoloration and history of repeated exacerbations.

DR. LEVIN stated that the case presented appeared to be Majocchi's disease because of the presence of purpura, atrophy and annular lesions.

GUMMA OF FOREHEAD IN A BOY WITH CONGENITAL SYPHILIS. Presented by DR. PAROUNAGIAN.

Irving P. A., a boy, aged 14, born in Russia, whose father and mother were both deceased, the cause of death being unknown, had a swelling on the right side of his forehead which, according to the boy's history, began six weeks previously. He could assign no cause for it, as he did not remember having fallen or having had any sort of injury. The condition was slightly painful when it first appeared, but later became painless. The lesion was as large as a walnut, and no signs of inflammation could be detected. The first Wassermann test revealed a one plus reaction, and the second was negative. He received an injection of neo-arsphenamin on November 5, and an injection of silver arsphenamin on November 8. The lesion was much improved after treatment.

DISCUSSION

DR. PAROUNAGIAN said that the history of six weeks' duration was the patient's statement, though he was inclined to believe that it was much longer. The patient had been seen by several surgeons, and various diagnoses had been made, among them cyst, sarcoma and lipoma. He stated that the patient had undisputed evidences of hereditary syphilis, with an imperfect hair line, extra sp. tubercle on the first molars, box-shaped skull, etc. Since the treatment with arsphenamin, the lesion had been reduced in size, and the negative or weak positive reaction might be accounted for by the mixed treatment which the patient had been taking before coming to the clinic.

COMPLETE DESTRUCTION OF THE PENIS, WITH TERTIARY SYPHILODERMS ON OTHER PARTS OF THE BODY. Presented by DR. PAROUNAGIAN.

H. S., aged 34, born in the United States, unmarried, said that he did not have a chancre. He said that he had had a gonorrheal infection ten years before, for which he had not consulted a physician. In 1917, an ulceration began on the under surface of the penis, near the frenum, which resulted in

a fistula. Gradually, the ulceration progressed until the glans penis was destroyed. The destructive process extended until another portion of the organ was destroyed. Finally, the remainder of the penis completely sloughed off, leaving an ulcerated area. At no time did he consult a physician until Oct. 29, 1923, when he had retention of urine, for which he was admitted to Dr. Keye's service at the Bellevue Hospital. He was later referred to Dr. Parounagian's department for treatment.

In addition to the destruction of the organ, he presented an artistic configuration of nodular patches on the upper portion of the chest and about the pubic region. The Wassermann test on Oct. 29, 1923, was four plus. The patient was given an injection of neo-arsphenamin, Oct. 31, 1923, an injection of silver arsphenamin, Nov. 5, 1923, and another injection of neo-arsphenamin on November 8.

DISCUSSION

DR. PAROUNAGIAN said that they were trying to heal the existing lesions. He had seen three cases of this kind, all about the same age, with similar histories. Two of the patients were married and one unmarried. One of the cases proved to be epitheliomatous. All of the patients appeared to be of extremely low mentality.

PSORIASIS IN A NEGRO. Presented by DR. PAROUNAGIAN.

Richard B., aged 42, colored, born in the United States, a carpenter, reported at the Bellevue Clinic, Feb. 11, 1924, with extensive and typical lesions of psoriasis of two months' duration. The lesions were situated on the scalp, extensor surfaces of the elbows and knees and elsewhere. They were itchy. He gave a history of a genital sore about twenty-three years previously, for which he had consulted a private physician, who gave him two bottles of medicine to take. In January, 1924, he consulted another physician, who had a Wassermann examination made, which was said to be positive. As this was the first case of psoriasis in a negro ever seen by the presenter, he thought it might be of interest to the other members.

DISCUSSION

DR. FOX said that it was difficult at times to distinguish between psoriasis and the papulosquamous syphiloderm. Psoriasis in the full-blooded negro was extremely rare. If this was a case of psoriasis, it was probably the most extensive and unusual one he had ever seen in a full-blooded negro. Psoriasis occurring in mulattoes was not so uncommon. He favored the diagnosis of syphilis in this case.

DR. GILMOUR agreed. He asked whether the scales had been scraped in this patient. Perhaps the bleeding hypertrophied papillae might help in making a diagnosis.

DR. ANDREWS discussed a case of inveterate psoriasis that improved temporarily under treatment with arsphenamin. The patient did not have syphilis. The therapeutic test would be valuable but not absolutely conclusive. If the case were inveterate psoriasis, one would expect this type of lesion to have required longer than two months to evolve. He favored the diagnosis of psoriasiform syphilis.

DR. FOX said that he thought this was a comparatively early type of syphiloderm on account of the extent and symmetry of the eruption. He felt that arsphenamin could be considered a satisfactory therapeutic test in such

a case, as in the vast majority of cases this drug had little or no effect on psoriasis. This fact had been established shortly after the introduction of arsphenamin.

Dr. Parounagian was of the opinion that the patient had a typical case of psoriasis, with usual involvement of the extensors of both extremities including the scalp, which showed typical silvery scales and marked itching. He had no clinical manifestations of syphilis, although he gave a history of a chancre twenty-three years previously. He did not consider the eruption of syphilitic origin, as the syphilitic skin manifestations of tertiary stage was not likely to be so generalized and symmetrical. He agreed to treat the patient with arsphenamin and mercury, excluding local applications; and would present him at the next meeting, to decide the diagnosis.

The patient was presented again at the March meeting of the society, and the following discussion took place.

Dr. Fox said that at the last meeting he had favored the diagnosis of syphilis. In view of the therapeutic test, however, which he thought adequate, he was willing to change his diagnosis to psoriasis. He had recently seen an almost similar case of extensive histologically proved psoriasis in a full-blooded negress. These two cases were unique in his experience, which included observations of a large number of negroes. The case mentioned by Dr. Ochs was by no means such a rarity as that of the patient presented, because he was a mulatto and not a full-blooded negro.

Dr. Wise agreed with the diagnosis of psoriasis.

Dr. Ochs said that he had not seen this case at the previous meeting, but he considered it psoriasis. He said that under no consideration would he consider syphilis. He called Dr. Fox's attention to a colored girl, photographed with lesions strongly resembling syphilis, but which turned out to be psoriasis, which cleared up nicely.

Nevus Anemicus and Psoriasis. Presented by Dr. O. L. Levin.

J. S., aged 25, a Russian, married, who came to this country seven months ago, one month after her arrival noticed a generalized eruption of psoriasis, which was still present. On the right cheek, she had a quarter of a dollar-sized, irregular, flat, nonelevated lesion, which was white and apparently free from blood vessels. This had been present since birth. Within this nevus, there were several pinhead to lentil-sized psoriatic lesions.

DISCUSSION

All agreed with the diagnosis.

Darier's Disease (Keratosis Follicularis). Presented by Dr. Oulmann.

Mrs. S., aged 52, about seven years ago, noticed some brown spots, crusted and oozing; also some red spots. None of these caused pain or itching. The lesions appeared at first on the breast, later below the breast on the right side of the abdomen and then in the axillary regions, extending to the back, and finally affecting the scalp in the left parietal region. Some of them looked like pigmented warts, while others could be removed by the fingernails, and left an oozing surface. The fresh lesions on the back showed a base with a mild erythema. The right breast was enlarged and hypertrophied. Some of the lesions healed, leaving white atrophic spots, and others a pinhead-sized

follicular infiltration. Under roentgen-ray treatment, the condition improved considerably, quarter unit doses having been given. No other member of the family suffered from any skin disease.

DISCUSSION

Dr. Wise said that he did not think one could make a diagnosis without a biopsy in this case.

Dr. Levin said that the lesions were more or less modified by roentgen-ray treatment which the patient had received, and which had also improved the appearance of the skin. However, in certain regions, as over the scapula, and in the temporal regions, there were distinct livid, papular lesions with thick, brownish, waxy plugs. He was of the opinion that the case was one of Darier's disease.

Dr. Oulmann said that if the members of the society could have seen the case before treatment, they would have seen the follicular implantation leaving the oozing surface and would have agreed with the diagnosis.

Duhring's Disease with Lesions of the Mucous Membrane. Presented by Dr. Wise.

F. C., aged 66, presented an eruption of three years' duration, showing a few vesicles and many papules. The skin itched, and the disease had a tendency to exacerbations and remissions. There were ulcerations in the mouth. The diagnosis of pemphigus was made by Dr. Fordyce several years ago.

DISCUSSION

Dr. Wallhauser agreed with the diagnosis.

Dr. Scheer said that this looked like a borderline case between dermatitis herpetiformis and pemphigus. The slight grouping on the shoulder and the good condition of the patient, plus itching, suggested Duhring's disease. In favor of pemphigus, however, were the lesions on the right tonsil and the fauces.

Dr. Ludwig Weiss stated that this patient would look much more emaciated if he had pemphigus, especially of the folliaceous type. He considered a case of such a type as incurable and fatal. As to the alleged identity of Duhring's disease and pemphigus, he was in doubt. The bullous diseases of the skin were far from being well defined clinically.

Sarcoid in Tertiary Syphilis. Presented by Dr. Andrews.

A woman, previously presented by Dr. Rosen with a diagnosis of syphilis resembling sarcoid, had a tertiary serpiginous syphilid of the neck with deep nodular infiltrations resembling sarcoid. Under mixed treatment the serpiginous lesions had disappeared, but the sarcoid-like infiltrations were unchanged. Arsphenamin had been avoided because of the possible effect of arsenic on sarcoids. It would now be given by Dr. Rosen, and the patient would be presented again by him after this treatment.

DISCUSSION

Dr. Wise said that he had seen this case twice before. The first diagnosis he had made was sarcoid in syphilis, the second was sarcoid in syphilis, and he made a third diagnosis this time of sarcoid in syphilis.

Dr. Levin said that he had seen the patient for the first time that evening. He said that clinically only two conditions could possibly be suggested; namely, paraffinoma and sarcoid of the Darier-Roussy type. Paraffinoma could be readily excluded, and he was of the opinion that the condition was sarcoid. The lesions were deeply set, firm and doughy, and could be picked up as if there had been a deposit of some firm material in the skin. There were no lymphatic enlargements, but what seemed to be a large cervical gland was only one of the sarcoid lesions.

Leukemid. Presented by Dr. Levin.

J. K., a man, aged 58, married, a custom house inspector, complained of a generalized, intensely pruritic eruption of ten months' duration. Examination of the skin two weeks prior to presentation showed a universal erythema with edema, vesiculation, crusting, fissuring and swelling of the skin. The edema was most marked on the face and hands. On the hands, it was so intense that the patient could barely pull his coat sleeves over them. The edema of the face was particularly marked on the eyelids, which showed puffiness and obliteration of the palpebral spaces. The skin of the forehead seemed to be elevated and distended with fluid, and seemed to be ready to rupture from pressure. The skin of the trunk also showed thickening and infiltration, while scattered over the back were numerous dime to half dollar sized, irregular, elevated, infiltrated, dark red and purplish patches. The patient showed marked improvement under technical coal tar and wet dressings, and when presented showed less intense edema of the hands and face, with a reduction of the infiltrated lesions of the rest of the skin. Follicular pustules and elevated, globular lesions had developed here and there. A piece of the skin from one of the infiltrated patches on the back was removed; there were chronic, inflammatory changes but no evidence of leukemia.

The laboratory findings were as follows: April 30, 1924: The blood Wassermann test was negative; red blood cells, 3,950,000; white blood cells, 25,000; polymorphonuclears, 50 per cent.; monomorphonuclears, 50 per cent.; hemoglobin, 70 per cent. May 3, 1924: red blood cells, 3,700,000; white blood cells, 32,000; polymorphonuclears, 46 per cent.; eosinophils, 11 per cent.; monomorphonuclears, 43 per cent.; hemoglobin, 65 per cent.; blood platelets, 204,000. Blood chemistry on April 27, 1924, showed: glucose, 0.1 per cent.; urea nitrogen, 18.4; creatinin, 1.1 per cent. The urine was normal except for traces of albumin and a few epithelial cells. Kidney function test — phenolsulphonephthalein — the first hour was 25; second hour, 9; total, 34. Stool examination revealed no parasites. The basal metabolism was 13 per cent. plus.

DISCUSSION

Dr. Levin said that he had presented the case, not as one showing frank leukemic infiltrations, but rather as one of leukemia with cutaneous lesions depending on the generalized metabolism disorder. The large infiltrations which had been pointed out had been present only for a few days. He was of the opinion that these infiltrations did not depend on a leukemic pathology, but resulted from infection of the hair follicles, producing inflammatory masses. Such inflammatory masses also occur in numerous other chronic skin disorders in which the normal resistance has been lowered and an invasion of the hair follicles by staphylococci has followed. A piece of tissue removed from one of the infiltrated patches on the back revealed no evidence of leukemia but merely showed chronic inflammation. The patient had been in the hospital

for about ten days, and during that time the only treatment he had received had consisted of wet dressings for the edematous parts, like the hands and face, and coal tar for the rest of the cutaneous condition. With reference to radiotherapy, Dr. Levin stated that this method of treatment would benefit the cutaneous conditions, whether they be only leukemids or true leukemic infiltrations. Such treatment would remove or improve certain symptoms, but it did not seem to have any real effect on the prolongation of the patient's life. This fact was recently emphasized by Dr. Minot in a paper published in *The Journal of the American Medical Association.*

XANTHOMA TUBEROSUM MULTIPLEX. Presented by DR. OCHS.

A man, about four months ago, noticed yellowish tumors appearing on both elbows; shortly after the onset, similar lesions appeared on the knees and infiltration on the arms. Some were starting on the abdomen, on the back of the scalp and on the back of the neck. There was some linear grouping.

DISCUSSION

DR. OCHS said that this case was seen for the first time three days prior to presentation. The patient did not understand English very well, and it was, therefore, difficult to obtain information from him.

DR. GILMOUR said that he would like to hear some suggestions for treatment.

DR. LEVIN said that the result obtained by Dr. Berkowitz in his case in which the patient was treated with palladium seemed to be marvelous, but he is now of the opinion that it was merely a matter of coincidence. Since observing the effect obtained by Dr. Berkowitz in his case, Dr. Levin had tried palladium in several cases of xanthoma tuberosum multiplex as recommended without any effect. In fact, it had been tried for two years in a typical case without any change in the lesions.

A CASE FOR DIAGNOSIS. PHENOLPHTHALEIN ERUPTION? Presented by DR. PAROUNAGIAN.

E. W., aged 31, born in the United States, a telephone inspector, married, when first seen on May 2, 1924, presented about ten pigmented patches of varying sizes, from 1 to 2 inches (2.5 to 5 cm.) in diameter, perfectly circular and most marked about the buttocks and genital regions. They first appeared one and one-half years ago after a nasal operation during which a local anesthetic was used. The condition began with intense itching, swelling and discoloration. The itching lasted about two days, and occasionally some of the patches became swollen and itched.

The second attack took place about one year ago without any appreciable cause and lasted one day. The patient stated that he had a "bleb" on the left side of the glans penis, which dried up without breaking (did not know whether there was any fluid in the bleb). The last attacks occurred during April, 1924, after taking "Bolls Rolls" and "Tangerine Laxative Tablets." On both occasions, the itching came on while he had the drug on his tongue. With the last attack, two new spots appeared accompanied by the same symptoms, itching and swelling, and lasted about two days, although the discoloration persisted.

The patient was troubled with spells of dizziness, numbness of the tongue and pain in the abdomen. The Wassermann test was reported negative on May 2, 1924.

DAVID L. SATENSTEIN, M.D., Secretary.

CHICAGO DERMATOLOGICAL SOCIETY

Regular Meeting, Nov. 19, 1924

JAMES HERBERT MITCHELL, M.D., *Presiding*

HYPERPIGMENTATIONS, HYPERTRICHOSIS AND MORPHEA. Presented by DR. ORMSBY and DR. MITCHELL.

A girl, aged 7 years, had an extensive pigmentation about the trunk and back of the neck, associated with morphea in the left epigastrium and a marked hypertrichosis. Her general health was excellent. The pigmentation was said to have started on the neck and to have been present for one and one-half years. The pigmentation had followed severe sunburn during the summer of 1923; the morphea had appeared in January, 1924. The hair had begun to grow rapidly on the arms during the past few months. The child was mentally precocious and was being kept out of school because she advanced too rapidly in her studies. The triad of disorders was apparently due to an endocrine imbalance.

DISCUSSION

DR. RICH (Salt Lake City) said that he recently saw a case of morphea in which the brown spots occurred, but not the diffuse pigmentation seen in this case. In his case, there were half a dozen brown spots, but the intervening skin was clear.

DR. SENEAR expressed the opinion that the pigmentation and hypertrichosis were suggestive of an endocrine disturbance, particularly of the suprarenals. He said that some dermatologists seem quite impressed with the endocrinous basis for severe hypertrichosis of this type.

DR. MITCHELL agreed with Dr. Senear regarding the endocrine origin of the disorder. He said that he expected to study the case further. In the absence of any investigative work, the child had been placed on 1/10 grain (0.006 gm.) of thyroid extract. She had apparently made some improvement during the past six weeks.

DR. FOERSTER asked what the patch on the trunk had felt like when the patient was first seen.

DR. MITCHELL said that it was perhaps somewhat thinner than when first seen. He suggested that it might be an involuting morphea.

DR. FOERSTER said he thought it was of interest that the pigmentation was found scattered through the patch in dots of follicular punctate pigmentation, which made it an unusual picture.

DR. RAVITCH recalled the case of a child about 4 years of age in whom the pigmentation was scattered over the entire body and neck. The case was also seen by Dr. Ormsby. The etiology and pathology of hyperpigmentation is so uncertain that one cannot give a real opinion. The child was placed on 1/8 grain (0.008 gm.) of thyroid extract, and this was continued for almost a year, but there was no improvement. He said that in his opinion, such cases were not curable. One can only say that they are of endocrine origin, if one cannot find the cause.

PIGMENTATION. Presented by DR. OLIVER.

A man, aged 29, had a pigmentation of the face that had been present for one year. He worked for the Western Electric Company, handling copper wire covered with oiled paper. Since stopping that work, his condition had

improved considerably. There were no subjective symptoms, and general physical examination was negative. The pigmentation was confined entirely to the face. There was no glandular enlargement or digestive disturbance.

DISCUSSION

Dr. Foerster said that the disorder in this patient was characterized by a peculiar mask-like pigmentation, with a sharp line of demarcation, and reticular pigmentation covering the upper eyelids. He received the impression that the case might belong in the group of pigmentations reported recently in continental Europe, called "war melanosis," and ascribed to chemical impurities in oil.

Dr. Finnerud said that if it was suspected that a metal had anything to do with the disorder, a section might show dissemination with the metal throughout the corium, particularly about the sweat glands, as in the case of argyria. Copper, by inhalation or other means, possibly would show up in this way, and such an examination might settle the diagnosis.

Dr. Senear said that he was reminded of the patient they presented last year who had a similar disorder. He was an athletic director who had a pigmentation which affected the temporal region. Since then it had taken on a more bluish tinge, and had spread over the face and forehead, with the same sharp line between the hair margin and the pigmentation which was present in this case. He believed Dr. Finnerud's suggestion was plausible.

Dr. Mitchell said he thought that if it were an argyrosis, the pigmentation would be more blue than this appeared. He believed it was more likely that it had been produced by an oil with which the patient worked.

Dr. Finnerud said that he had seen some sections and moulages of Riehl's melanosis, but he knew very little about it. Physicians in Europe appeared to have rather an indefinite conception of this rare disorder.

Dr. Mitchell said that, about a month ago, they had seen a Russian girl who had well defined areas of pigmentation on the face, which appeared at intervals. When she was first seen, there was a sharp line of demarcation over the forehead, but when she came in again the pigmentation had almost entirely disappeared. It was more red than dirty brown, and the patient said it had been recurring for several years. He suggested salicylic acid to produce an exfoliation, since the process seemed to be superficial.

Dr. Oliver said that the patient had improved a good deal since he had changed work. The pigmentation was not nearly so marked, and the general physical condition was good.

Sarcoid. Presented by Dr. Ormsby and Dr. Mitchell.

A man, aged 52, first shown at the December, 1923, meeting, was presented again at this time to show the improvement manifested under arsenical therapy following a recurrence in October, 1924. He was given six Asiatic pills a day. The lesions had largely involuted during the past six weeks.

A Case for Diagnosis. Presented by Dr. Hedge for Dr. Stillians.

A woman, aged 28, a native of the United States, was first seen in June, 1924, when she had five small tumor-like growths beneath the skin, one on the flexor surface of the right forearm, three on the flexor surface along the radial aspect of the left forearm, and one on the anterior surface of the right thigh. None of these growths was painful, but the one near the right elbow

was tender to palpation. The growths varied in size from that of a small hazelnut to that of a walnut, were freely movable and were somewhat harder than the usual consistency of lipomas. The one near the left elbow was the largest, and was elevated above the surface of the skin; the others were flat and plaquelike. The Pirquet and Wassermann reactions were negative.

The patient had received 5 drops of solution of potassium arsenite (Fowler's solution) three times a day, and the growths had markedly decreased in size under this therapy. Because of gastric irritation, the solution had to be stopped, and she was given 0.3 gm. neo-arsphenamin, followed by Asiatic pills, but her improvement had not been so rapid as before.

DISCUSSION

Dr. Hedge said they were particularly interested in the marked decrease in the size of the tumors following arsenical therapy. They thought the case might be one of the atypical types of sarcoid.

Dr. Harry R. Foerster said that he thought the tumor in the right arm was a lipoma, whereas the tumors in the left arm were more superficial, seemed to involve the cutis and suggested the possibility of sarcoid. In his opinion, the statement of Dr. Hedge that the lesions had diminished in size under arsenical therapy would substantiate the diagnosis of sarcoid.

Atrophia Pilorum. Presented by Dr. Ormsby and Dr. Mitchell.

A girl, aged 2 years, with a history that at 4 weeks of age the hair, which had been thick at birth, fell out and at the same time she had a number of styes, continued to have occasional boils, but eventually a sparse growth of hair developed. When first seen, she had an impetiginous eruption on the face. The older children in the family were said to be normal, but the mother had had eczema in childhood.

The entire scalp was covered with a scanty growth of hair, averaging about 1 cm. in length. All of the follicles of the scalp were conspicuously keratotic, as were also the follicles on the body, but to a much lesser degree. The hairs of the scalp were medullated, uneven in diameter but not definitely bearded as in monilethrix. Occasional nodes could be seen, but these were found microscopically to be due to fracture. Examined in glycerin, the hairs appeared to be twisted. The brows were devoid of hairs, but the lashes were about 2 cm. long and curled backward, forming two complete loops. There was no bony deformity, the nails were unchanged and the child was mentally alert and intelligent. The father and mother were excellent physical specimens.

DISCUSSION

Dr. Ebert said that his impression on examining with a direct light on the specimen was that the hair was twisted, and not exactly circular but oval. He had attempted to make some sections in the ordinary way to ascertain definitely whether it was oval but had not yet succeeded. He hoped to get some cross sections of the hair and discover the real condition. In his opinion, there were no real strictures but simply twists in the hair.

Dr. Oliver recalled two cases which he had presented two years before in boys 12 and 16 years of age. Both had marked alopecia, with the same type of hair seen in this case. There was pronounced keratosis pilaris of the scalp and keratosis on the body. At that time, a number of the gentlemen present discussed the cases with the idea that the disorder might possibly be of endocrinous origin. They took the youngest boy to the hospital and kept him there

for two months, testing him in every way as to his metabolism, but they did not secure a section of the scalp. The tests were all above normal, and the boy was much brighter than the average child. He also had two very large front teeth, but there were no spoon nails. At that time the cases were classed as being of the congenital alopecia type described by Dr. Hyde as alopecia congenitalis, with spoon nails. He wondered whether this case might belong in the same group.

LYMPHANGIOMAS OF EYELIDS. Presented by DR. ORMSBY and DR. MITCHELL.

A woman, aged 51, had lesions about the eyelids that had been present for thirty-five years, and which had always been considered cysts. They had been removed surgically several times but recurred, according to the patient, unless they were removed without breaking the sacs. The lesions were large, pea-sized, hemispheric, translucent, thin-walled sacs containing a watery fluid of neutral reaction. The sacs collapsed completely when ruptured. She had been under observation since Sept. 18, 1924, and had received a series of treatments with the roentgen ray.

DISCUSSION

DR. FOERSTER said he thought it was a case of hydrocystoma.

DR. SENEAR said that he thought of lymphangioma and hydrocystoma when he saw the patient, and was inclined to the first diagnosis until he talked with Dr. Foerster, and then he thought it was hydrocystoma.

NODULAR SYPHILIS. Presented by DR. STILLIANS.

A woman, aged 53, a native of the United States, on the back of the right hand and wrist had the segments of a circle 14 cm. in diameter and two others 8 cm. and 2 cm. in diameter, respectively. The lesions formed as short segments which broke into shorter portions as they lengthened. The border was from 1 to 2 mm. wide, smooth, pink and elevated 1 mm. She gave a history of having had symmetrical keratoderma of the palms and soles since the age of 9 years.

The Wassermann reaction was strongly positive.

DISCUSSION

DR. MCEWEN said that a case was shown at the Cleveland meeting in October which was almost identical with this, but the lesions were in a different location and of longer duration. The lesions were strongly suggestive of tertiary syphilis, but it was decided that it was a superficial form of lupus. The Wassermann reaction was negative, but it was nevertheless difficult to differentiate the case from syphilis.

DR. EISENSTAEDT said that in view of the positive serum reaction, the fact that the lesions were only slightly elevated and pale, and since there was no definite evidence of tuberculosis, he thought the case was one of tertiary syphilis. He had seen several similar cases which had cleared up under antisyphilitic treatment, in which the diagnosis between syphilis and a trichophyton infection was difficult.

DR. O'LEARY said that he thought it was a superficial cutaneous syphilid.

DR. SENEAR said that they had a similar case under observation in a patient who had some apparently ecthymatous lesions on the leg. The case was regarded as ecthyma until the patient exposed the left leg, on which there was

a lesion similar to that presented today, annular in outline and about the size of a butter plate, involving the posterior surface of the leg. This had cleared up under mercury and potassium iodid therapy. The clinical picture was the same as that in this case.

DR. ZEISLER said that he thought it was a not unusual type of late syphilis.

DR. STILLIANS said that the patient had treated herself for ringworm for six months, and when he first saw her the lesions were painted with iodin. He was impressed, however, with the fine ridge at the border and the size of the lesions. The patient said the lesions always appeared as segments of circles, never as single lesions.

ADENOMA SEBACEUM. Presented by DR. FINNERUD and DR. OLIVER.

A boy, aged 10 years, had had an eruption on the face for five years. Six other children in the family were said to be unaffected and normal. The mother said that when the eruption began, the lesions were smaller and less numerous, but presented a similar appearance to those now present. One lesion of the scalp had been present since birth, and one on the forehead had been present for five years.

Histologic section of the scalp lesion showed a chronic hyperplasia of the collagen and increased vascularity of the pars papillaris. There was also a cyst, apparently of sweat gland origin, in one portion of the section.

DISCUSSION

DR. ZEISLER asked about the mentality of the patient.

DR. MITCHEL said the case was interesting because of the nevus-like lesion on the brow which is so often seen in these cases. He had a photograph of another child with adenoma sebaceum with an almost identical lesion on the forehead.

DR. FINNERUD said that the child was bashful but was normal mentally. There were six other children in the family, and all were said to be normal. He thought it was interesting that an associated nevus could be of any type, that it need not nesessarily be a hemangioma. In this case, there was a fibrous tumor in the scalp. He asked for suggestions as to treatment.

DR. STILLIANS suggested radiotherapy.

DR. FOERSTER suggested the use of the cautery or fulguration as therapeutic agents. He had never used them, but believed they might be of value. It has been found that in some of these cases there is an associated malformation of the brain stem, described as tuberous sclerosis by the neurologists, which is of interest in connection with those who have adenoma sebaceum and who also exhibit an abnormal mentality.

PERIADENITIS MUCOSA NECROTICA. Presented by DR. HEDGE for DR. STILLIANS.

A woman, aged 26, first seen on Oct. 28, 1924, at that time had marked reddish patches on the lateral portions of the tongue which she said caused burning and some pain, especially at the time of onset. They had been a source of annoyance and a menace to her health, because she was unable to eat while they were in the acute stage. The trouble had been present for more than twenty years. Her tonsils had been removed two years before presentation. There was no history of herpes zoster, but she had had labial herpes on several occasions.

A tentative diagnosis of Moeller's glossitis was made, but on her return, the picture was considerably changed. There were then three lesions on the left cheek, one on the left side of the tongue, one on the left side of the upper lip and five on the right cheek. Each lesion was made up of an area of erythema with a central necrotic patch, somewhat depressed. The necrotic portion, if seen soon after its formation, could be removed as a solid mass, more resembling a core than a membrane, but removal was difficult a day or two after its formation. The lesions persisted for from six days to six weeks before complete healing occurred. There was no scar formation.

DISCUSSION

Dr. Senear said that the history of definite plugs being extracted might make one accept the diagnosis, but from the standpoint of the clinical picture at present the case was only a stomatitis. These cases are interesting because they are so difficult to cure. They had seen several similar cases recently, and Dr. Schamberg saw one of the patients in consultation in June. He recommended the use of an autogenous vaccine made from the variety of organisms which they obtain from the smears in these cases. In the reported proceedings at a recent meeting of the Philadelphia Dermatological Society, Dr. Schamberg or one of his men brought this out when a case was presented.

Dr. Zeisler agreed with Dr. Senear that many patients have recurrent canker sores for years, and they are difficult to overcome. So far as he knew, Dr. Sutton was the first in this country to describe the condition called "periadenitis mucosa necrotica," but he thought the lesions in Sutton's cases were much more deep-seated than those in the present case. He could see no evidence of necrosis in this case.

Dr. McEwen suggested that the case be tested out with ipecac. The value of ipecac in the treatment of pyorrhea is well known, and he thought it might be possible that the organisms in the lesions were related to those in pyorrhea.

Dr. Mitchell said he wondered what effect emetin would have.

Dr. Rich said that he thought it was an ordinary case of aphthous stomatitis which occurs throughout life.

Dr. Mitchell said he and Dr. Ormsby had had a medical student under observation for some time who had had these lesions for many years and who was never free from them. He had had all sorts of bacteriologic work done, the gastro-intestinal tract thoroughly examined, and had received many different kinds of treatment, all to no avail. Individual lesions would clear up in a week and others would appear, very much like herpetic lesions. Apparently, they were at first vesicular lesions on an inflamed base. They had recently given him some arsphenamin. At first, there was nothing more than a reaction from the drug without any effect on the lesions themselves. After the third injection, the lesions cleared up, and the patient had remained free for the past week.

Dr. O'Leary said that they had seen a considerable amount of thrush of the mucous membranes lately. Culture for *Oidium* had been negative, although on section the organisms were demonstrated in the corium. He thought the lesion presented by this patient closely resembled lesions of aphthous stomatitis and did not resemble lesions of thrush. He could not agree with the diagnosis of periadenitis mucosa necrotica recurrens.

A Case for Diagnosis. Presented by Dr. Stillians.

A negress, aged 25, was first seen on Sept. 8, 1924, at which time she had a mild type of acne involving the face, shoulders and upper arms. She gave a history of a similar attack eight months before, at which time she consulted a physician in Georgia, who administered six intravenous injections (neoarsphenamin), two in the left arm and four in the right. The left arm was swollen and tender for seven or eight days following one of the injections. The last treatment was received about April, 1924. No Wassermann test was made. No itching was complained of, and the lesions were said to appear at various intervals. When examined in September, no pigmentation was observed. Two Wassermann tests made within two weeks were 2 plus. The patient was then given six intramuscular injections of sulpharsphenamin at weekly intervals. After the sixth treatment, examination revealed a bluish-black pigmented area about the size of a silver dollar in the left cubital region, two semicircular areas on the upper part of the arm, bands about one-half inch (1.2 cm.) wide extending partly around the arm in the region where tourniquets are often applied, and similar but smaller and less well defined lesions in corresponding locations on the right arm. The patient said that she had taken no medicine except Epsom salts and mineral oil, and had used no local applications. There were no lesions about the buttocks, where the intramuscular injections had been given.

DISCUSSION

Dr. Zeisler called attention to the two linear pigmented bands around the arms which might have been due to the pressure of a constrictor, and the other areas of pigmentation he thought might have been due to the local effect of the intravenous injections she had received.

Dr. Senear called attention to a short linear patch at the right elbow, where the pigmentation was centered in an old scar from a needle puncture.

Dr. Stillians said the interesting thing to him was that the intravenous injections were given in April, and the pigmentation did not appear until after the intramuscular injections of sulpharsphenamin were given. There was no preliminary treatment with mercury by mouth or otherwise. He believed an histologic examination might show something.

Psoriasis. Presented by Dr. Waugh.

A boy, aged 11 years, who was presented at the October meeting with lesions of the palms and soles, had a follicular eruption that had developed on the body within the past month. A microscopic section taken from the leg was exhibited.

DISCUSSION

Dr. Zeisler considered the case one of psoriasis.

Dr. O'Leary said that when the patient was seen last month he thought the disorder was mycotic, but now the psoriasis seemed definite. The associated follicular lesions did not fit in with the psoriasis, and suggested the possibility of a trichophytid. He believed further observation necessary to reach a conclusion.

Dr. Eisenstaedt said he thought it would be interesting to determine whether there would be any improvement in the small keratotic lesions if the arsenical therapy were discontinued. He believed the arsenic might be precipitating the keratosis.

Dr. McEwen said that he was not entirely satisfied as to the nature of the condition, although he was willing to concede that it might be psoriasis. He thought Dr. Eisenstaedt's suggestion regarding arsenic was good.

Dr. Harry R. Foerster said that he was of the opinion that the keratoses over the sternum were present when the boy was presented at the October meeting. He believed the condition was psoriasis, and that the keratosis were not related to the lesions on the palms and soles.

Dr. Finnerud said that he did not know how to account for the lesions on the body. Some of them looked like the early lesions of psoriasis, and the distribution was proper for that disease. He could not account for the patches of lichenoid papules which were most marked on the front of the trunk. He thought the lesions on the palms and soles were typical of psoriasis. The microscopic section on exhibition was taken from the leg by Dr. Montgomery. The section was so clearly one of a moderately infiltrated lesion of psoriasis that it required no description. He believed that no one would take exception to that histologic diagnosis.

Dr. Foerster called attention to the sharp limitation of the infiltrate as seen in the section.

Dr. Mitchell said that he was among those who did not see psoriasis in the case when the patient was presented before, and he thought it was difficult to make a diagnosis with the lesions on the palms and soles in the stage they were at that time. There were bullous lesions with up-turned scales which strongly suggested a mycotic process, and it had been impossible for him to say what the condition was. The patient was seen in the office by Dr. Finnerud and Dr. Ormsby on Sept. 20, 1924, and Dr. Ormsby had had no hesitation in calling the condition psoriasis. The history was that of psoriasis.

Dr. Montgomery said that the patient had been taking arsenic for two months, and the keratotic lesions were noticed on the body during the past two weeks. He said in regard to the infiltration that the specimen showed a lymphocytic type of cells around the hair follicle and also some infiltration around the sweat glands, which do not accompany psoriasis.

NEW YORK DERMATOLOGICAL SOCIETY

Regular Meeting, Nov. 25, 1924

Hans Jorgen Schwartz, M.D., *President*

Lupus Erythematosus with Nodular Lesions Suggesting Sarcoid. Presented by Dr. Fordyce.

A girl, aged 20, at the age of 12, had had a lesion on one cheek, which was at first diagnosed as ringworm, but which afterward developed into a typical lupus erythematosus. The original lesion extended to the bridge of the nose and to the other cheek. Later, she developed subcutaneous nodules involving the cheek in the neighborhood of the lupus erythematosus lesions. At the same time, nodules appeared in the subcutaneous tissue of the arm near the shoulder. These lesions afterward underwent involution and left depressed scars. The case was presented because of the coexistence of the two conditions — one a typical lupus erythematosus, the other probably sarcoid. In Dr. Fordyce's opinion, the two conditions were due to the same cause.

DISCUSSION

Dr. Howard Fox said that the depressed scars were strikingly similar to those in the case that he had reported as one of sarcoid, and in which both he and Dr. Wise had treated the patient. Some of the lesions had been treated by the Finsen lamp and others by carbon dioxid snow. The patch on the nose appeared to be a lupus erythematosus.

Dr. Highman said that he was glad to see this case, for it substantiated an opinion he had long entertained about the relationship of lupus erythematosus to other diseases that produced the same general effect. He was satisfied that the process belonged among the primary atrophies, for the loss of substance was mainly in the subcutaneous tissues in this case. He wondered whether there was not some relationship between lupus erythematosus and the macular atrophies. Unquestionably, it was some type of restricted atrophy in a patient with lupus erythematosus, and the two types of lesions were due to some relationship in this case, not to two separate conditions.

Dr. Wise agreed with the diagnosis.

Dr. Trimble said that the case fitted in with his clinical idea of sacroid. He had seen several patients with frank lupus erythematosus associated with sarcoid. Whether or not the cases were all sarcoid and not lupus erythematosus, he did not know. The deep sunken scarring was rather characteristic of sarcoid. As Dr. Fox said, it was similar to a case they had seen together some years before. In his opinion, this case could be classified with the Darier-Roussy type of sarcoid.

Dr. Williams said he thought the question was one of etiology. Lupus erythematosus was a symptom and sarcoid was a symptom. Both conditions were probably due to an infection — perhaps with tuberculosis, perhaps with tuberculosis and some other infection. In this case, the hidden infection seemed to be producing two varieties of external lesion instead of one.

Dr. Fordyce, referring to what had been said about the two conditions being due to the same cause, said that the atrophic scarring seemed to be out of proportion to the original lesions and would indicate that there was more tissue destruction than would be expected on account of the sharply circumscribed nodules. He thought that the same process which had produced the lupus erythematosus had produced the others.

Dr. Clark, referring to Dr. Fordyce's remarks, said that was probably true of these cases of sarcoid. He then told of a typical case of sarcoid in which the patient had a tremendous amount of atrophic scarring, and he had had a great deal of trouble in persuading her not to bring suit on account of the disfigurement, which was out of proportion to anything that radium could have produced. Radium would clear up these cases, but it was well to warn the patient of the marked atrophy that might result, not from the radium treatment, but from the lesion itself.

Livedo Reticularis? Presented by Dr. Williams.

Two sisters in a family of seven were affected — the third and fourth children; the others were normal. Each presented a mottling of the skin, at the age of 18 months, which soon spread to the areas involved at the time of presentation, and remained stationary. Both girls were underweight and undernourished. The intellect of both seemed to be all right. There were no positive pathologic findings. The children suffered from chronic diarrhea, which was

stopped by drugs, but which recurred as soon as the drugs were omitted. The skin presented the condition on both cheeks, on the backs of the hands, on the buttocks and on the legs, the centers of involvement fading into the surrounding skin. The skin of the two girls did not tan as did that of the other children in the family.

The children had been under observation for a year, and no satisfactory diagnosis had been made. The nearest diagnosis seemed to be livedo reticularis. There were no cardiac and no pulmonary lesions.

DISCUSSION

Dr. Wise said that he thought the eruption might be classed with the livedo reticularis group, but that it differed from the typical cutis marmorata in the absence of reticulated network of vessels, which represented the bases of vascular cones in the skin. He regarded the affection as belonging in the nevus family.

Dr. Trimble said that he thought the condition was evidently brought out by exposure.

Dr. Highman said that whereas this patient had not the definite earmarks of Hutchinson's disease or Majocchi's disease, nevertheless, the case tended to establish the fact that he had maintained for a long time — that all telangiectatic dermatoses, including Schamberg's disease, are closely related. This case seemed to be an example of the kind that belonged in that group, although it did not fit in with any of the classical pictures. It was another group in which the relationship of its components would have to be carefully studied. His first impression was that this was a case of angioma serpiginosum; although it did not fit in with the general picture of that disease, it had enough of its features to warrant the belief that it was not remote from this category.

Dr. Williams said that the diagnosis of angioma serpiginosum was considered and ruled out, for the telangiectases were not the main feature of the cases; there were only a few spots on the body and on the nose in which any dilated blood vessels were perceptible — it was rather a broad patch of erythema. He believed it was a nevoid condition, as suggested by Dr. Wise, some congenital weakness of the blood vessels, but more than that he could not say. It seemed to belong to the livedo rather than to the telangiectatic group. It was a rather broad mottling. The etiology was unknown. He had not been able to find anything like it in the literature.

Pellagra. Presented by Dr. Wise for Dr. Fordyce.

L. S., a widow, aged 44, had suffered from the condition for four weeks. She had had diarrhea for about two weeks preceding the outbreak of the skin lesions, which were of an eczematous character, distributed over the arms, hands and parts of the face. She had recently been drinking large quantities of alcohol in the form of cheap gin, and dated the beginning of the trouble shortly after several weeks of drinking. The patient presented an extensive ulceration on the ventral surface of the tongue, which extended from the tip of the tongue to the frenum and which was about three-quarters inch (1.9 cm.) wide. It had a greenish-yellow surface. The entire tongue had a beefy red appearance. The flush area of the face was dark tan and was highly erythematous and scaly. The sebaceous gland follicles were prominent. The dorsa of the hands and all aspects of the wrists presented an erythematous,

pigmented, moist eczematous eruption, which was sharply marginated at the anterior aspect and ended a few inches beyond the wrists, and which was symmetrical. On the anterior surface and on the side of the neck was an erythematous, scaly, somewhat lichenified eruption about an inch (2.5 cm.) in width and arranged like a collaret. The patient felt weak and looked sick. There was a loss of appetite and an incessant diarrhea; also there was mental aberration of a mild type.

Dr. Trimble agreed with the diagnosis. The most interesting point was that the lesions appeared comparatively suddenly, following the ingestion of cheap alcohol. That was an especially interesting feature.

Dr. Highman said the condition looked like pellagra.

Dr. Howard Fox said that he thought the case might prove to be one of pellagra, although he did not think it a classical eruption. The fact that the dermatitis on the hands was of the moist variety did not exclude that diagnosis.

Dr. Kingsbury said that he did not think it was a case of pellagra. The dermatitis was rather superficial and not sharply demarcated. He had seen several similar cases in the City Hospital which were cases of alcohol poisoning. The history of the ingestion of gin was suggestive. In his opinion, it was a dermatitis brought out by drinking.

Dr. Fordyce said that he was inclined to believe that the diagnosis made by Dr. Wise was correct. He had seen several cases of pellagra in and about New York City in patients whose diet was not restricted. It was possible that such patients selected from the diet only carbohydrates. He believed with Dr. Goldberger that pellagra should be classified with the diseases caused by a food defect rather than as an infection.

Dr. Whitehead said he thought that the two most classical symptoms — absolute symmetry and sharp limitation — although absent in this case, would not rule out pellagra. This was apparently a rather late case, and there was a tendency for these symptoms to disappear. The ulcerative stomatitis, the collaret and the associated diarrhea undoubtedly made the diagnosis of pellagra correct.

Dr. Wise said that the points brought out by Dr. Whitehead would indicate that the diagnosis was correct. Besides the skin condition, the patient had a severe diarrhea, and she had recently exhibited signs of mental deterioration.

Sarcoid or Sarcoma. Presented by Dr. Howard Fox. (Previously presented.)

Mrs. C. L., aged 65, was first presented in April, 1923, as having a case of sarcoid. In May, 1921, two reddish tumors on the face had been treated by the roentgen ray, the larger having existed for twenty years. Both lesions had disappeared after a single treatment, and had not recurred up to the present. In April, 1923, two other smaller lesions were again treated by roentgen ray, the lesions disappearing promptly and remaining well up to the present time.

DISCUSSION

Dr. Highman said that when he had seen the patient four years before, he had thought that she had sarcoma, and he was still inclined to the same belief and for the same reasons, despite the history of long delay in recurrence. The lesion appeared too glassy and waxy for sarcoid; it looked like the condition seen in neoplasms, and this was the main reason for regarding it

as sarcoma. However, that was simply an impression. It looked like sarcoma, even though there was no other reason for believing it to be sarcoma.

Dr. Howard Fox said that the biopsy which had been made formerly was not successful, as a cautery had been used to excise the tissue. No positive diagnosis could therefore be made at present. He still felt that it probably was not sarcoma on account of the long duration of the lesions (twenty years) and the long period of quiescence since the treatment by roentgen ray.

Lichen Planus Confined to the Mouth. Presented by Dr. Howard Fox.

Mrs. R. I., an Italian woman, aged 49, had suffered for the past year from an eruption confined to the mouth. It had attained its maximum development at the end of several months, and had since remained stationary. Her attention was called to the eruption by a mild amount of irritation, which was especially noticeable after eating. The lesions were present on the buccal mucosa, affecting especially the interdental clefts. In addition, there was a narrow strip of an eruption, apparently of the same type, along the right side of the dorsal surface of the tongue, and a superficial whitish scaling on the vermilion border of the lips. The eruption was fairly profuse and consisted of superficial whitish lesions of delicate structure. Some of the lesions were discrete and appeared as pinpoint papules; others, having apparently coalesced to form diffuse areas, had a more or less reticulated appearance. There was no enlargement of the contiguous lymphatic glands. A thorough examination of the entire surface failed to reveal any evidence of an eruption. The patient gave no history of syphilis, and she had never smoked. She was accustomed to drink wine occasionally. She was short and stout and in apparent good general health.

DISCUSSION

Dr. Fordyce said that in his opinion the diagnosis of a primary lichen planus of the mouth was probably correct. He hesitated, however, to make a diagnosis without the coexistence of lesions on the skin. He reported a case of a primary lichen planus on the tongue in a patient who was not a smoker and had never had syphilis. Subsequent observations confirmed this diagnosis.

Dr. Williams said he thought the condition was lichen planus, and told of two cases he had observed — one in which there were lesions on the tongue only and one in which there were lesions on the tongue and on the inside of the cheek. These patients had been under the care of Dr. Pollitzer for lichen planus five or six years ago.

Dr. Trimble said that he was inclined to agree with the diagnosis, although there was an element of doubt.

Dr. Wise said that he thought the case had all the features of lichen planus of the mouth.

Dr. Pels (Baltimore) said that he was interested in what Dr. Fordyce had said. He had recently seen two cases of lichen planus of the tongue, both associated with a few lesions on the body. In one case, there were lesions on the glans; and in the other, that of a woman, there were typical lichen planus lesions on the arms. The lesions on the tongue were profuse and striking in view of the slight involvement of other parts. It would be interesting to know how frequently this combination occurs, namely, a considerable involvement of the tongue and mucous membranes of the mouth together with so

little of the disease on areas of the skin. Furthermore, it had been his experience that a profuse distribution of lichen planus on the body and extremities was usually unaccompanied by lesions in the mouth, and if these are present under such conditions they are few in number. He was curious to know whether this had been the experience of members of the Society.

DR. HIGHMAN said that he thought the condition was lichen planus; it looked like it and was disseminated as it would be. During the last three or four years, he had seen at least half a dozen cases of lichen planus of the buccal orifice that in two or three instances had been confirmed by the presence of characteristic lesions elsewhere on the body.

Replying to Dr. Pels' question, Dr. Highman said that one point had been answered already; in generalized lichen planus, a majority of the cases showed buccal involvements, though not nearly so extensively as in this case — but an amazing number did not have any mucous involvement. One would expect it to be an invariable finding, but it was not.

DR. BECHET remarked that the woman had a large number of typical lichen planus lesions on the lower lip; a leukoplakia did not occur in this location. The lesions on the mucous membrane consisted of whitish, grouped, pinhead sized dots. In his opinion, the diagnosis as presented was correct, even though there were no lesions elsewhere. He had recently presented before the society a reticulated fish-net-like lichen planus of the mouth, but in this case there were also lesions on the glans penis.

DR. HIGHMAN said that in this particular case one of the points was that the lesions did not look like leukoplakia but more like typical lichen papules.

DR. FORDYCE said that in case of doubt it was always possible to confirm the diagnosis of a primary lichen planus of the mouth by an examination of a small piece of tissue which could be readily removed with a cutaneous punch.

LUPUS VULGARIS ERYTHEMATODES (LELOIR). Presented by DR. HOWARD FOX.

G. A. P., aged 36, an automobile salesman, a native of New Brunswick, Can., during the year following September, 1920, had suffered from six attacks of erysipelas of the nose and cheeks. Each attack lasted about a week and was accompanied by fever and other constitutional symptoms, often confining him to bed for a few days. For two years previous to these attacks, he had suffered from nasal catarrh and had undergone an operation for removal of bone from the nose. The eruption presented had first appeared in September, 1921, affecting the nose at the outset and later the cheeks. About one year before presentation, it had attained its maximum development. He had been treated by scarification, electrolysis, vaccines, and by liquid air — all without appreciable result. There had been no subjective symptoms, and his general health had remained good. A piece of tissue had been previously excised and examined histologically by a general pathologist in Montreal. A probable diagnosis of lupus erythematosus had been made at that time.

On examination, the eruption was seen to occupy the entire surface of the nose, extending on both cheeks to form a typical bat-wing configuration. There was some destruction of the right ala, giving the nose a slightly beak-like appearance. There was also a small area of semisoft tissue suggestive of lupus vulgaris. The general color of the eruption was bluish red. Numerous telangiectases were present on both nose and cheeks. The areas on the cheeks showed a diffuse, fairly firm infiltration, with nothing to suggest the nodules of lupus vulgaris. A piece of tissue was excised under local anesthesia from

the left cheek and a section made by Dr. J. Frank Fraser. It showed the presence of a few small but unmistakable tubercles composed chiefly of epithelioid cells. There was nothing to suggest lupus erythematosus.

DISCUSSION

Dr. Fordyce said that on superficial examination the case might be mistaken for lupus erythematosus, chiefly because of its site. On careful examination, however, the deep infiltration of the tissues of the cheek which was present in this case was not a picture of lupus erythematosus. Furthermore, the wing of the nose presented a distinct loss of tissue and also showed a few typical lupus nodules.

Dr. Fraser said that, histologically, it was a case of lupus vulgaris. He did not know of any organism except the tubercle bacillus that produced typical epithelioid tubercles in the corium. In this case, the tubercles were situated principally around the hair follicles. The presence of deep-seated conglomerate tubercles would account for the clinical features.

Dr. Bechet said that the biopsy settled the diagnosis, but that clinically he did not think the case conformed to the Leloir type of erythema-tuberculous lupus. The lesions were confined to the nose, and were distinctly nodular and protuberant; they had the characteristic "apple jelly" color. The mass on either side of the nose was deeply indurated, but with the exception of the telangiectasia, the overlying skin did not show the characteristic superficial tuberculous lupus as described by Dubreuilh, Vidal and Leloir; it seemed more like a chronic cellulitis or lymphatic stasis. The lesions on the nose were typical of lupus vulgaris.

Dr. Kingsbury said that from the history of the case and the appearance of the cheek, he would not be inclined to regard the condition as a lupus, either vulgaris or erythematosus. The condition was undoubtedly caused by the intranasal trouble. The man had had so-called attacks of erysipelas, etc. The condition of the cheek, particularly where the biopsy was not made, was due merely to congestion, with marked telangiectatic change.

Dr. Trimble said he thought that Dr. Kingsbury's explanation was correct, but there was no doubt about the "apple jelly" lesions on the nose. He agreed with the other speakers that it probably came from the condition in the nose — a tuberculous focus, etc., which caused a lymph blocking, followed by the condition on the cheeks and around the alae of the nose where the bacillus found suitable soil for producing the effect shown.

Dr. Wise agreed with Dr. Trimble, i. e., that the condition was due to a tuberculous infection in the nose, causing a blocking of the lymph vessels and providing a suitable soil for the production of the indurated lesions of the cheeks.

Dr. Highman said that several points had been brought out in the discussion: in the first place, clinically and from a distance, the condition looked like Leloir's type of lupus so far as color and site were concerned; the intumescence of the lesions was against lupus erythematosus and in favor of lupus vulgaris. If it was this, it was the type described by Leloir, as was pointed out by the presenter. Clinically and histologically, he thought it would have to be classified as lupus vulgaris. In the condition as discussed by Dr. Kingsbury, there was a different microscopic picture, hyperplasia of the connective tissue and a chronic lymphatic engorgement, both of which were lacking in the slide from this patient, so that the condition Dr. Kingsbury

alluded to could be ruled out. There was no microscopic evidence of its being a chronic recurring lupus erythematosus. As to the relation of the infiltrations to the sebaceous and hair structures of the skin, Dr. Highman disagreed with Dr. Trimble's remarks about this being a curious finding, as if it were possible for any condition on the face to avoid these structures. As to the remarks about the "apple jelly" nodules, although in this particular case it would indicate lupus vulgaris, it was not invariably such an induction. In lupus erythematosus, one saw similar yellowish puncta due to elastic tissue degeneration. Finally, although believing this to be lupus vulgaris, Dr. Highman pointed out that in the sarcoid of Boeck, tubercles were the elementary lesions, as in lupus vulgaris. In his last article, Boeck pointed this out and suggested the name miliary lupoid for the condition named for him. It was conceivable that the lupus erythematosus of Leloir was the equivalent of Boeck's miliary lupoid.

Dr. Clark said that he thought there were two distinct processes, and told of a case shown some time before, presenting the characteristic picture of the edema on the face of this man. This condition cleared up after a number of months under hot boric acid fomentations, leaving no trace behind. Dr. Clark thought that the patient under consideration had lupus vulgaris. It would seem that the inflammatory edema of the cheeks might not be connected with the lupus vulgaris.

Dr. Howard Fox said that with the aid of the histologic section which had just been made, the diagnosis was plain. Previous to this, however, the diagnosis had been difficult to make from the clinical standpoint. Solid edema of the face (elephantiasis) following attacks of erysipelas had been considered, but was discarded on account of the inflammatory appearance of the eruption. Some points in the case suggested lupus vulgaris, while in general the appearance was more like that of lupus erythematosus. The fact that a general pathologist had found no evidence of tuberculosis in the sections strengthened the case against lupus vulgaris. The speaker had been fortunate in excising tissue which showed a definite structure of tuberculosis, which clinched the diagnosis.

Exfoliative Dermatitis. Presented by Dr. Williams.

W. M., aged 38, said that his trouble began in June, 1921, when large red blotches appeared on his legs and arms. This was followed by great groups of boils—in all, he had between 700 and 800 at that time. In January, 1922, an inguinal gland removed by Dr. Fordyce apparently showed mycosis fungoides. A skin section taken somewhat later did not show mycosis fungoides, but neither did it rule out that condition. He was treated with the roentgen ray, arsphenamin and arsenic in various forms, with great improvement. In February, 1922, numerous blood and skin tests were made at the Presbyterian Hospital, all of which were indecisive—the Wassermann reaction was negative; the blood contained eosinophilia only. He was first seen by Dr. Traub in September, 1924, at which time he was exfoliating from head to feet, a condition that had existed for four months previously, in spite of constant treatment by Dr. Dearborn, who had been giving him injections, probably of arsenic. He was given injections of 1 gm. of sodium thiosulphate in 10 c.c. of distilled water. In all, he received seventeen injections, but the condition practically cleared up with the exception of his legs, after the first seven or eight injections. After discontinuing the thiosulphate, his skin remained clear for about two weeks, since

which time he had gradually developed red, slightly indurated blotches, covered with scales, all over his body. He had improved during the past two or three days when he was again put on thiosulphate, this time by mouth.

The Wassermann reaction was negative. It was a question whether the case was one of leukemia cutis, mycosis fungoides or just recurrence of the exfoliating dermatitis.

Biopsy slides were shown by Dr. Williams.

DISCUSSION

DR. TRIMBLE said that he did not think such a condition could be discussed until after a prolonged study. He had seen several similar cases, one of which resembled this case markedly; and after keeping it under observation for about five months, the patient developed a large fungating tumor, and the condition proved to be mycosis fungoides.

DR. WISE agreed that the differential diagnosis in the absence of altered blood findings was difficult in a case of this kind. The diagnosis of mycosis fungoides on microscopic examination of the glands of the groin was subject to discussion; he did not, however, think the man had mycosis fungoides or ever would have, and he suggested the diagnosis of pityriasis rubra of Hebra.

DR. HIGHMAN shared Dr. Wise's opinion as to the difficulty of reaching a definite conclusion, but was himself inclined to think the condition was mycosis. It did not look like pityriasis rubra of Hebra for the same reason that one butterfly did not look like another. At the Mount Sinai Hospital, there was a case of exfoliative dermatitis following injections of arsphenamin. As time went on, nodules developed on the shins, together with a general glandular enlargement, although the original exfoliation disappeared. Now the man had a thickened skin. One of the lesions showed definitely histologic evidences of mycosis or of a closely allied condition, leukemia having been ruled out by the blood picture. Dr. Highman said that he did not see how any one could express a definite opinion about a case of this kind except in the course of time.

DR. BECHET said he also thought it was impossible to make a definite diagnosis. He would not have thought of mycosis fungoides; there were no sharply defined plaques and apparently no infiltration. The clinical picture was that of a generalized erythroderma, and in his estimation somewhat resembled an atypical leukemia cutis.

DR. FRASER said he thought that time alone would bring about the solution; one would have to wait to see what developed. He was inclined to agree with Dr. Wise that it was a case of pityriasis rubra of Hebra.

DR. CLARK suggested that the condition might be an arsenical dermatitis pure and simple. What condition the man may have had before was an open question. A patient with this condition had been in the Skin and Cancer Hospital two or three years ago; before that he had had recurrent attacks of dermatitis herpetiformis; since his last trip, he had been actively treated with arsenic. He had taken a lot of Asiatic pills and solution of potassium arsenite (Fowler's solution) up to high doses, and presented a picture almost typical of the condition shown by the patient under discussion. After repeated doses of sodium thiosulphate, his condition was markedly improved. As soon as these injections were stopped, he would revert, and the eruption would become more prominent. Each time he was found to be eliminating considerable quantities of arsenic. Apparently, the condition was going to clear up under sodium thiosulphate therapy.

NEVUS INVOLVING SOFT TISSUES AND BONY STRUCTURE OF THE FACE. Presented by DR. WISE for DR. FORDYCE.

J. G., aged 12, presented a lesion on the side of the face and the scalp which had been present since birth. At the age of 3 months, she had been operated on, and part of the growth had been removed surgically. She presented a long scar on the right side of the face, extending from the temple across the cheek to and involving the upper lip. Over the malar eminence was a puffy swelling about the size of a hen's egg, involving the lower lid. The underlying bony structures were markedly hypertrophied. This had been present since birth and was said to be less prominent than formerly. A similar soft swelling was located on the scalp just beyond the hair line in the median portion, which was hemispherical and about 2 inches (5 cm.) in diameter. The soft palate presented a prominent, irregularly shaped soft swelling which projected into the buccal cavity. The pharyngeal wall on the left side was markedly hypertrophied, and the structure showed considerable distortion.

DISCUSSION

DR. CLARK said he thought that an interesting point was the distinct bony deformity along the central line of the forehead—a decided bony enlargement on the right side of the nose.

PARAPSORIASIS (LICHENOID TYPE). Presented by DR. HOWARD FOX.

T. D., aged 57, born in Ireland, a fireman, had lived in the United States for the past forty years. No member of his family had suffered from a similar disease. He was married and had six children, all of whom were living and well. The eruption, which had been present for eighteen years, had first been noticed on the fingers and toes, gradually extending centripetally on the forearms and arms and feet. It was still continuing to spread. There had never been any appreciable itching.

Examination showed an eruption involving principally the flexor surfaces of the forearms and lower thirds of the arms and the dorsal surfaces of the feet, extending about an inch (2.5 cm.) above the ankles. It consisted of superficial, slightly scaly, light yellowish-red, dry, nonitchy patches. Scattered through the eruption were small areas of normal skin, giving the eruption a reticulated appearance. Many of the lesions were of a lichenoid character, none of them, however, being characteristic of lichen planus.

Histologic examination made by Dr. J. Frank Fraser showed the presence of a simple dermatitis, with no suggestion of lichen planus or lichen scrofulosorum. The report stated that: "The vessels appeared contracted and surrounded by a cellular exudate (chiefly of the round cell type). There is an absence of the granular layer in some places and in other places it showed hyperplasia. The exudate was confined to the papillary layer. Diagnosis: Chronic dermatitis (parapsoriasis)."

A CASE FOR DIAGNOSIS: PARAPSORIASIS? Presented by DR. WILLIAMS.

The case was presented as a companion to the one shown by Dr. Fox. The lesion was on the right arm and of three years' duration.

DISCUSSION

DR. FRASER said that Dr. Fox's case was one which illustrated the importance of interpreting the histopathologic findings in the light of the clinical

picture. From a study of the slide alone, he would hesitate to make a diagnosis, but after seeing the patient and correlating the microscopic and clinical features, he was convinced that it was a case of parapsoriasis.

Dr. Bechet said that he thought the lesions in Dr. Fox's case resembled a parapsoriasis lichenoides. In Dr. Williams' case, the lesions were more distinctly lichenoid; they were shiny and isolated, particularly on the forearms. It well exemplified the fact of the close resemblance to lichen planus of some cases of parapsoriasis of the lichenoid type. Both cases, however, were examples of the same disease, parapsoriasis lichenoides.

Dr. Trimble said he thought that the two cases were identical, but that Dr. Williams' case looked more like lichen planus than any other condition he had ever seen; although he agreed with the diagnosis of parapsoriasis, he had never seen a case of that disease that was not generalized. These cases were limited to the hands and feet, did not itch, had the proper color—slightly pink; the reticulation and apparent atrophy would all fit in with the symptoms of parakeratosis variegata. That, according to Brocq's classification, would be parapsoriasis lichenoides.

Dr. Wise said that he had the impression that both cases were parapsoriasis—as Dr. Trimble had said, parakeratosis variegata. Histologically, the slide under the microscope was indistinguishable from the sections of which they had a large number in the Vanderbilt Clinic—parapsoriasis en plaques. He thought the diagnosis of one case was confirmed histologically.

Dr. Highman agreed with Dr. Wise, and said that in the clinical appearance of the case and its indeterminate histologic aspect lay the greatest evidence in favor of parapsoriasis.

Dr. Howard Fox said he thought it was astonishing to see two unusual cases presenting an almost perfect similarity of appearance and location. The most likely diagnosis by a process of exclusion, from both the clinical and the histologic standpoint, was that of parapsoriasis.

Lichen Planus Linearis. Presented by Dr. Wise for Dr. Fordyce.

H. T., a negress, aged 19, born in the United States, presented a linear arrangement of verrucous papules extending from the dorsum of the left hand along the arm and over the left shoulder, and ending on the left scapular region. The whole averaged one-quarter inch (0.6 cm.) in width. These papules were also slightly scaly in places, and in others had shiny tops. There were two similar linear patches, one on the right thigh and the other on the right leg, the latter starting at the knee and running downward. Both of these patches were about 8 inches (20 cm.) long and one-half inch (1.2 cm.) wide. The mouth presented a gingivitis, and the lips small ulcerative lesions. The outer side of the right thigh was pigmented from a previous attack, presumably of lichen planus. No itching was present. The Wassermann test was negative. A biopsy was made, which had not yet been studied microscopically.

Note.—The lesions on the lips cleared up after treatment of the gums by the dentist, and probably bore no relation to the lichen planus of the skin. The buccal mucosa exhibited no signs of the eruption.

DISCUSSION

Dr. Howard Fox said he thought that the linear lesion presented the appearance of lichen planus. At all events, this was one of the diseases which

at times assumed a linear configuration. The eruption on the thigh certainly appeared to be lichen planus in process of retrogression.

Dr. Highman agreed with Dr. Fox that the linear lesions looked like those of lichen planus.

Dr. Pels (Baltimore) agreed with the diagnosis of lichen planus.

Dr. Fraser said that he thought the diagnosis of nevus unius lateris should not have been considered. The lesions in this case were not verrucous. They were smooth and in other respects typical of lichen planus.

Dr. Trimble said that he agreed with the previous speakers in regard to the linear lesions, but asked what the lesions on the mouth were. They were evidently not lichen planus. He would like some light on that question.

Dr. Wise said that he had knowledge of two cases diagnosed clinically as lichen planus linearis, but which on histologic examination proved to be types of verrucous nevi.

Leprosy. Presented by Dr. Wise for Dr. Fordyce.

A mulatto, aged 21, born in the United States, presented patches of depigmentation on both knees and on the arms and back. These patches varied in size from that of a pea to 3 inches (7.6 cm.) in diameter, the largest being on the knees. All of them showed a slight degree of anesthesia. The pea-sized patches, of which there were six, were located on the back, and here they showed a slight degree of atrophy. The epitrochlear glands were palpable, and there was a suggestion of ulnar nerve thickening. The Wassermann test was negative. There was no loss of eyebrows and no other symptoms. The nasal secretion examination for the lepra bacillus had not yet been made.

Granuloma Inguinale. Presented by Dr. Howard Fox.

D. W., aged 26, a full-blooded negress, a native of Savannah, Ga., had lived in New York for the past two years. She had been married for twelve years, had had one child (living and well) and one miscarriage (five years before presentation). She gave no history of syphilis. For the past three years, she suffered from leukorrhea. In November, 1923, an ulcer which bled freely appeared on the vulva and disappeared spontaneously in January. About three months later, the present eruption appeared and continued to spread until two months ago, when it became stationary. A physician had previously given her three injections in one arm and two in the gluteal region, without benefit.

Examination showed an ulceration involving the lower portion of the left labium majus and, contiguous with it, an ulceration on the labium minus. The first mentioned lesion measured three-quarters by half an inch (1.9 by 1.2 cm.), the second lesion being somewhat smaller. The borders were elevated and rolled, and the surface of the ulcers was covered with yellowish-red indolent granulations. The ulcers were slightly tender. There was a silght enlargement of the left inguinal glands. The Wassermann test was negative. A piece of tissue from the ulcerated surface was excised under local anesthesia, and smears from the deeper parts were made. A sparse number of clumps of Donovan bodies were found, some intracellular and some extracellular. The same tissue was used for histologic examination by Dr. J. Frank Fraser, who reported the presence of a granuloma which would fit the diagnosis of granuloma inguinale. Smears showing the Donovan bodies, and the histologic section were demonstrated.

KERATODERMA AND RADIODERMATITIS. Presented by DR. WISE for DR. FORDYCE.

A married woman, aged 52, had been suffering for two years with a thickening of the skin of the palms and soles. So far as she knew, she had received no injections of arsenic nor had she taken arsenic internally. A few months following the appearance of the change in the skin, she had received twelve roentgen-ray treatments on the palms at weekly intervals. A few months later, there had appeared on the palms, pigmentation, telangiectasia, keratosis and epitheliomas. The plantar surface of the heels, which had not been exposed to radiation, also exhibited a moderate degree of hyperkeratosis.

NEW YORK ACADEMY OF MEDICINE, SECTION ON DERMATOLOGY AND SYPHILIS

Regular Meeting, Dec. 2, 1924

PAUL E. BECHET, M.D., *Chairman*

PEMPHIGUS. Presented by DR. WOLF.

H. M., aged 54, presented an eruption which had existed for three months. The patient, who had been under observation for eight weeks, had been shown at the October meeting of the Section, and by request was presented again.

DISCUSSION

DR. POLLITZER said he had seen the case two months previously, had accepted the diagnosis then, and still held that opinion. The eruption seemed to be somewhat under the control of the medication at present.

DR. WISE said that he wished he were as sure as Dr. Pollitzer that it was pemphigus, for he felt that he could not make up his mind in such a case. The man showed no lesions in the mouth, was apparently in good health, and the lesions were stellate in outline. The picture was not that of pemphigus, but rather more like Duhring's disease without itching. In his opinion, the question could not be decided without observing the patient for some time to come. Of course, Dr. Wolf had had the man under observation for a long time, and his opinion should be considered, but the condition resembled Duhring's disease more than true pemphigus.

DR. SCHEER, who had seen the case at the previous presentation, said that he then regarded the condition as pemphigus. As Dr. Wise had said, it now looked more like Duhring's disease. The grouping of the lesions was not evident at the former presentation. Whether or not this change was due to the medication received, he could not say.

DR. PAROUNAGIAN agreed with the diagnosis.

DR. BECHET said that he had seen the case in Dr. Trimble's service at the Bellevue and University Clinic. At that time there were fewer lesions and the skin was irritable, a considerable amount of dermographism being present. There were also distinct papules scattered among the vesicles and bullae; for these reasons, he had felt inclined toward the diagnosis of erythema multiforme bullosum, and he still favored that diagnosis. He agreed with Dr. Wise that the case was not typical of pemphigus. At the same time, one could not be dogmatic in the diagnosis of a bullous eruption; in its early stages, a definite

opinion was frequently impossible. The question of whether or not there were bullous lesions in the mouth, had no bearing on the diagnosis; it was possible to have a frank pemphigus without lesions of the mouth. In recapitulation, the patient had an extensive bullous eruption bearing considerable resemblance to a bullous erythema multiforme; whether or not this eruption would become pemphigoid, was a matter for the future to decide.

Dr. Pollitzer said that any one who had seen many cases of pemphigus would have seen a number that began like this one, going on for a while with a little hesitation, and then developing frankly into a condition which would be recognized as pemphigus.

Dr. Wolf said that the case was of three months' duration. From the start, the primary lesion was a bulla; the bullae would dry and form crusts. What was now seen was the end stage of the lesions that had appeared from the time the patient first came under observation. The lesions were all over the body, and were dried bullae. The crusts that the man shed every night were large in amount. There was no grouping, but what was seen was just where the former lesions had been. He could not reconcile a dermatitis herpetiformis with such an extensive eruption which was without any polymorphism or itching, and he did not see how the condition could be called anything but pemphigus. The patient did not present the terminal lesions — namely, mucous membrane involvement — which would clinch the diagnosis. As for medication, he had received sodium arsenate, 2 per cent. solution, up to 20 minims. The kidneys were being watched carefully, and the amount would be reduced if necessary.

Dr. Wolf said that he would be glad to have any suggestions for further treatment. When he first saw the case, three days after the eruption appeared, he had made a tentative diagnosis of erythema multiforme or possibly pemphigus. The man had not been treated by any one else, so far as he knew, and had not received arsenic.

Dr. Pollitzer said that he saw in this discussion what the Freudian psychologist would explain as a desire to escape from the diagnosis of so grave a disease as pemphigus. For the past three months, this man had had a succession of bullae arising on a clear skin, without itching. As for grouping, one might pick out a number of the lesions and by connecting them with lines one could derive any kind of geometric pattern; but there was no grouping of the lesions in the ordinary sense. Against the diagnosis of dermatitis herpetiformis was the absence of polymorphous lesions, pain or itching. The man had bullous lesions without any other symptoms. If the eruption was not pemphigus, one would have to change the name of that condition.

Dr. Levin confirmed what Dr. Pollitzer had said about pemphigus, and stated that at the previous meeting when the patient was presented, he had agreed with the diagnosis of pemphigus. At the second presentation, the lesions were only more marked and more extensive, and he was more certain than ever that the diagnosis was correct. There was no grouping of the lesions. They were only more numerous, and therefore seemed to be grouped. The patient would probably develop lesions in the mouth later.

Reinfection in Syphilis. Presented by Drs. Parounagian and Mason.

C. C., a man, aged 24, unmarried, born in Cyprus, a tailor, had been admitted to the Bellevue Syphilis Clinic on July 21, 1924, and at that time showed multiple lesions on the prepuce, of fourteen days' duration. On July 23, the

dark-field examination for *Spirochaeta pallida* was positive. The Wassermann tests were negative on July 21 and 28. He received eight arsphenamin and fifteen mercuric salicylate injections — beginning July 28 and ending November 3 — and was instructed to return on December 15 for another Wassermann test.

The patient returned on November 17 on account of a new lesion on the dorsal aspect of the prepuce, said to be of twelve days' duration. After careful questioning, a history of exposure five and a half weeks prior to the appearance of the new lesion was obtained, which was indurated and sharply outlined. The dark-field test was positive on six examinations. The Wassermann tests made on November 20 and November 25 were both negative. The Wassermann specimen taken on December 1 had not yet been reported on.

DISCUSSION

DR. CHARGIN was inclined to accept the case as one of reinfection. While the patient did not present all the criteria necessary to establish the diagnosis of reinfection, the import and facts were present. The sore and positive *Spirochaeta pallida* findings warranted a diagnosis of syphilis. The case was still in the pre-Wassermann period; hence the treatment could be considered adequate to cure the case completely. The history of exposure, the appearance of a sore, clinically typical of a chancre, not at the site of the sore of the first infection, and the finding of many *Spirochaetae pallidae,* plus an adenopathy, warranted this being considered a new infection.

DR. WILLIAMS said that he was very much interested in the subject of reinfection, but it seemed to him that a great many words were wasted about it. This man undoubtedly had had syphilis; he apparently had received fairly efficient treatment, and the Wassermann findings were negative. He may or may not have been cured. As a matter of fact, no one knows whether any one has ever been cured of syphilis. The patient then exposed himself, and, the Wassermann test remaining negative, he developed a sore containing spirochetes. If he had been cured, reinfection occurred; if not, superinfection.

DR. THORNLEY said that what was not evident was that the patient had had an opportunity to become reinfected with syphilis. Was the source of infection examined, or was it just an ordinary exposure with no positive evidence of syphilitic or other infection?

DR. PAROUNAGIAN said that the first case of reinfection which he had presented before the Academy at the January, 1915, meeting had been discussed in the same manner. He hoped to be able to prove the diagnosis in this case also, as the patient was not receiving any treatment for his second infection. Referring to a statement made about repeated Wassermann tests, he said that besides the September 22 Wassermann test which was negative, at least two other Wassermann tests had been made, with negative results. As to Dr. Thornley's question in regard to proving the source of infection, Dr. Parounagian asked in how many instances he had been able to do that.

DR. RULISON said that he had had the pleasure of working for three years in Dr. Parounagian's large clinic for syphilis, and time after time cases had been brought up from there reported as superinfection, and this same discussion had recurred. It seemed somewhat unfair. Dr. Parounagian had an extremely large clinic, and saw a great many rare cases. During the last fifteen years, the treatment of syphilis had been greatly improved, and there seemed to be reasonable grounds for hoping that some patients had been cured. If that were a reasonable probability, it would seem evident that every such

case that came under observation was well worthy of serious discussion. If a criterion of cure were to be established, it was on just such cases that the criterion must be based. In this particular instance, it seemed that there was every element on which to prove a reinfection. The only thing was to wait for a later Wassermann reaction, and possibly that might be obtained.

SECONDARY SYPHILIS WITH UNUSUAL DESTRUCTION OF ROOF OF MOUTH (PREVIOUSLY PRESENTED AS BALANITIS GANGRENOSA). Presented by DRS. PAROUNAGIAN and MASON.

W. D., aged 26, admitted to the Bellevue Syphilis Clinic on Sept. 17, 1923, then had a lesion on the prepuce, near the sulcus, of two weeks' duration. The period of incubation was uncertain. As the man had applied iodin, six dark-field examinations were negative. During his attendance, the sore became gangrenous, and he was made an indoor patient. The lesion progressed, gradually destroying as much as two thirds of the organ. At first, the Wassermann examination was negative, but later it became positive, and antisyphilitic treatment was energetically administered. The records showed that he received twenty injections of arsphenamin, four of neo-arsphenamin, five of a proprietary sulphur preparation, three of silver arsphenamin, and eighteen of mercuric salicylate. In addition, he received sodium iodid intravenously, and iodids by mouth. In spite of all this treatment, the condition progressed, so that the entire roof of the mouth was destroyed. The edges of the ulceration were cauterized by silver nitrate solution, and peroxide mouth washes, etc., were employed. The perforation began about the early part of June, 1924.

DR. SATENSTEIN said that the case very much resembled cases of Vincent's infection, and he had the impression that there was some additional infection in the mouth causing the tremendous destruction.

DR. PAROUNAGIAN, referring to Dr. Satenstein's query "Why call it secondary when the lesion is tertiary?" said that he did so because the infection occurred a little more than a year ago, and up to two years after infection it was customary to classify such cases as the secondary stage and after that as tertiary. The patient was presented as having a case of secondary syphilis with tertiary manifestations. As to the suggestion of Vincent's infection, Dr. Parounagian said that he could not reconcile himself to that diagnosis because the man had received enough arsphenamin to eradicate a dozen Vincent's infections; besides, he did not believe that Vincent's disease could cause that amount of destruction. Replying to Dr. Goodman's question, he stated that the young man was born in New York City, was a truck driver and had never been in tropical countries.

Dr. Parounagian presented the case because he had never before seen such extensive destruction in spite of the amount of treatment; he also hoped for therapeutic suggestions.

A CASE FOR DIAGNOSIS. Presented by DR. LEVIN.

A. S., a man, aged 60, married, stated that he had had the lesion presented for more than six years. On the dorsa of the toes of the right foot, there were several discrete lentil-sized to pea-sized, elevated papular lesions. These tended to group themselves and form patches in segments of circles. They were coppery red, and covered with thick layers of dirty, grayish-white scales. Lesions characteristic of psoriasis were found on other parts of the body. The patient gave a history of having had gonorrhea thirty years prior to presenta-

tion. He had never taken arsenic, but complained of greatly increasing deafness of two years' duration.

Dr. Abramowitz remarked that all the lesions were keratotic with a granulating base, something like a gonorrheal keratosis. The patient had had gonorrhea some years before. He ventured a provisional diagnosis of gonorrheal keratosis.

Dr. Wise said that he did not know what the diagnosis might be. The tendency would be to call all the lesions psoriasis. The patient had psoriasis on the elbow. At one of the Philadelphia meetings, he had seen a case of angiokeratoma on the toes, and it seemed possible that this might be the same condition.

Dr. Rulison said that the patient had a rather curious history of treatment. He had come to the clinic nine months before with red, keratotic formations like corns between the toes, much thicker than as presented. The diagnosis was rather puzzling, and the man was given Whitfield's ointment, after which the condition cleared up rapidly, the lesions entirely disappearing. At the same time, the man had, on the lower part of the sacrum, scaly, nondescript lesions which might have been psoriasis, but also might have been tinea or some other condition. They also cleared up under treatment with the ointment. The history was that these lesions had been present for six years. The man had had gonorrhea once, thirty-five years previously. The lesions on the elbow had not appeared until two months before presentation.

Dr. Scheer would have been inclined to the diagnosis of psoriasis but for one thing. On removing the crusts or the hyperkeratosis on one of the lesions of the toes, an elevated rounded projection was left; he had never seen this in psoriasis, where the surface is flat, on a level with the surrounding skin; here was a distinct elevation, rather spherical. That seemed useful in ruling out psoriasis.

Dr. Levin said that the patient had first appeared at the clinic nine months prior to presentation, and the lesions were then considered to be dermatophytosis. They improved rapidly under treatment with Whitfield's ointment. The presence of the copper colored papules with the peculiar grouping suggested the possibility of syphilis. Dr. Wise's suggestion as to the possibility of angiokeratoma should be seriously considered. Of course the patient showed lesions of psoriasis on other parts of the body, but he did not consider the lesions on the toes to be similar in nature.

Lupus Erythematosus. Epithelioma? Presented by Dr. Levin.

E. P. K., aged 51, married, a clerk, stated that he had had the lesions for a period of more than five months. The eruption first appeared as small, slightly elevated, red spots, which gradually became more elevated and extended more deeply into the skin, and enlarged to form large masses and round patches. The chin presented several pinhead-sized to pea-sized, elevated, firm, dark red papules and tubercles. The older lesions showed a tendency to become confluent and enlarge peripherally to form dime-sized lesions, which were annular and shaped like a horseshoe. The central areas in the larger lesions showed scarring, while the border was elevated, dark red, firm and hard, and covered with thin, firmly adherent, grayish-white scales. On stretching the borders, they presented a pearly appearance. The left side of the neck presented a silver-dollar sized area, which was made up of discrete and confluent papules

and tubercles, below which there was a slightly elevated, dark red mass the size of a hazelnut, which infiltrated the tissue deeply and showed scaling as well as scarring. The right auricle presented characteristic red patches with dilated pilosebaceous follicles, filled with thick horny masses and showing the firmly adherent grayish-white scaling of lupus erythematosus. A similar but less marked condition was present in the left auricle. The general medical examination revealed no clinical evidence of tuberculosis. The Pirquet and the subcutaneous tuberculin tests were negative, as was also the Wassermann test. The urine was normal. A roentgenogram of the skull, taken because of the severe headaches of which the patient complained, showed no abnormalities.

The pathology will be reported on later.

DISCUSSION

Dr. Pollitzer said the lesion in the concha of the right ear was characteristic of lupus erythematosus; he considered the other lesions on the face and neck to be of the same general nature, through the type (infiltrated nodular) was different. The association of various types was not uncommon.

Dr. Wise agreed with Dr. Pollitzer that the whole condition was probably lupus erythematosus, but suggested that Dr. Levin have a histologic examination made of the nodular lesions; he would probably find a structure of benign miliary lupoid or sarcoid. He said that association was becoming more and more prevalent, and more cases were being seen and diagnosed as nodular lupus erythematosus in which the microscopic examination showed the structure of sarcoid. As to the other diagnosis, he had read every article on the subject he could find, and was still very much in the dark as to the actual appearance of lesions of Bowen's dermatosis; he had seen no appearance of any such lesions as he had read descriptions of, and he did not think that the diagnosis of Bowen's precancerous dermatosis should be considered in a case which so closely resembled lupus erythematosus.

Dr. Bechet agreed with what Dr. Wise had said about the concomitant occurrence of lupus erythematosus and sarcoid. It had seemed to him that this association had been observed more frequently of late.

Dr. Levin stated that the patient presented characteristic lesions of lupus erythematosus, but also showed lesions which were made up of confluent papules which arranged themselves in groups forming segments of circles. The borders, when pinched, showed a rolled, pearly appearance, which, together with the annular arrangement of the lesions, suggested the possibility of Bowen's disease. A piece of tissue was to be removed, and a report would be made on the pathology at the next meeting.

The microscopic pathology of an infiltrated lesion showed lupus erythematosus.

Epithelioma. Presented by Dr. Levin.

T. E., a man, aged 37, unmarried, presented a lesion on the left hand, which had existed for eleven years. It has first appeared as a small, red, moist spot, and had gradually enlarged to the present size. It became slightly painful and tender, and showed a little hardness with pustulation along the borders. As presented, there was a superficial flat ulcer about 3 inches (7.6 cm.) long and one and a half inches (1.27 cm.) wide, involving the web and adjacent surface of the ring and middle fingers of the left hand. This lesion looked bright red, was moist and fairly sharply defined. It seemed to be tender, and on palpation it was found that the proximal part was hard and stonelike. There was also

scar formation. On trying to move the lesion on the deeper tissues, it was found to be more or less fixed and difficult to move from the bone. Examination of a piece of tissue from the proximal border revealed the presence of epithelioma, possibly having its origin from the inner sheath of the hair shaft (Huxley's layer).

DISCUSSION

DR. SCHEER called attention to the superficial type of epithelioma described by Graham Little, which he called erythematoid epithelioma, clinically erythematous patches something like those in this case, exceedingly superficial.

DR. LEVIN remarked that clinically the condition suggested a moist eczema, except where the border at its proximal end presented a hard infiltration. Microscopically, the lesion was a basal celled epithelioma.

NEVUS. Presented by DR. SCHEER.

J. G., a girl, aged 12, had been presented on a previous occasion. At the age of 3 months, she had been operated on by a surgeon for a congenital condition involving the right side of the face. She now presented a long scar extending from the temple down across the right cheek and involving half of the upper lip. Over the malar eminence was a puffy swelling involving the lower lid. This had been present since birth, and was said to be less prominent than formerly. A similar swelling of the same consistency was present on the scalp just behind the hair line of the forehead, near the midline. A smaller swelling extended from the hair line to the bridge of the nose. A similar swelling involved the entire soft palate on the right side, and there was a deformity of the hard palate.

DISCUSSION

DR. WISE said that the patient had presented herself at the clinic with the hope and expectation that something might be done to improve her appearance. She had a lesion on top of the scalp which might be an angioma or a lipoma. There was an involvement of the malar bone, and the question was whether a second operation would be indicated, and whether it would be advisable to excise in the same scar on account of the tendency to keloid formation. Dr. Wise said that he would be very glad to receive any suggestions as to the best mode of attack to secure improvement in appearance; also as to whether radium should be used on the palate.

DISCUSSION

DR. WOLF said he thought that this particular case was not in the province of dermatology, and that a good plastic surgeon might suggest something to improve the cosmetic appearance of the patient.

DR. SCHEER said the patient had been operated on at a very early age by Dr. Willy Meyer. The father stated that there was considerable improvement.

PHENOLPHTHALEIN ERUPTION. Presented by DR. LEVIN.

L. C., a woman, aged 30, married, stated that for about two years she has been having recurrent attacks of red spots over the anterior aspect of the wrists. She had formerly lived in the tropics, and had had attacks of ringworm. When she first appeared at the clinic, she presented on the fronts of both wrists two annular lesions, having a border about one-fourth inch

(0.06 cm.) in width, which were scaly, dark red, slightly vesicular and showed telangiectasia. The central areas were only slightly reddened. The front of the right wrist showed a half-dollar sized oval, dark red, scaly, elevated patch. On close questioning, she admitted having taken various forms of cathartic pills at different times. Because of the dark red and purplish color and the telangiectasia, a phenolphthalein eruption was suspected. About twenty-four hours before presentation, the patient had taken two phenolphthalein tablets in the form of Ex-Lax, and within twelve hours the lesions became more pronounced, more elevated and more inflamed, and the patient complained of burning sensations and intense itching on the site of the lesions.

DISCUSSION

Dr. Abramowitz said the eruption had a peculiar ringed appearance such as he had not before seen attributed to phenolphthalein. Another factor was conceivable as having changed the picture, and that was the application of some external remedy. His first impression was that the case looked like a maculo-anesthetic leprosy, but Dr. Fox had tested it out carefully, and there was no anesthesia. The most important point was that the lesions flared up twenty-four hours after the test dose of phenolphthalein, which, to his mind, was proof positive that the rash was due to phenolphthalein.

Dr. Williams told of a case presented last year, that of a boy aged 10 or 12, showing signs of Fröhlich's syndrome, with an extensive phenolphthalein eruption occurring in large plaques with erythematous borders, and also in rings, simulating erythema multiforme.

Lupus Erythematosus? Ulerythema Ophryogenes? Presented by Dr. Rostenberg.

In a brunette, aged 20, during the winter of 1922, reddish lesions appearing simultaneously on the scalp and face, accompanied with itching. The patient presented five areas of alopecia from 2 to 4 inches (5 to 10 cm.) in diameter, the surface being glistening and white, and showing slight atrophy; a few broken off hairs were still present. In the middle of the occiput, there was an area about 3 inches (7.6 cm.) in diameter, beginning in the hairy scalp and extending down to the neck, dark red, covered with grayish, adherent scales, and showing marked atrophy in spots. On the right temple and extending over the right eye, brow and lid there was a bandlike reddish patch, slightly atrophic and scaling. There was marked thinning of the hair on the eyebrow on its outer half. There were no horny projections on the hair follicles.

DISCUSSION

Dr. Wise said he believed that all of the lesions were caused by lupus erythematosus.

Epithelioma on the Inner Aspect of the Little Toe. Presented by Dr. Parounagian.

A colored woman, aged 40, born in the United States, gave a history of syphilis contracted four years previously, for which she had received several arsphenamin injections. She applied at Bellevue Syphilis Clinic on Nov. 1, 1924, on account of a sore on the inner lateral aspect of the small toe of the left foot, the duration of which was said to be about ten weeks. The sore was

sharply marginated, perfectly round and elevated. The patient complained of considerable pain. The Wassermann test taken on Nov. 24, 1924, was reported negative, and she showed no active manifestations of syphilis.

DR. PAROUNAGIAN said that a corn was first considered, although as the lesion was elevated, sharply circumscribed, mushroom-like in appearance and accompanied with considerable pain, he was inclined to regard it as a case of epithelioma. He would have a biopsy made and report on it later.

SECONDARY SYPHILIS WITH EXTENSIVE CONDYLOMAS IN A NEGRO. Presented by DR. PAROUNAGIAN.

W. J., a man, colored, aged 40, who came to the Bellevue Syphilis Clinic on Nov. 29, 1924, stated that about four months previously he had had several sores on the inner surface of the prepuce. The history given was unsatisfactory, although he remembered having an eruption over the entire body about one month after the sores appeared on the genitals. He had numerous condylomas about the penis, scrotum and inner aspect of the thighs. There were no lesions about the anal region. A Wassermann test had been made, but the result had not yet been reported. As the case was typical, treatment was begun immediately.

MEATAL CHANCRE: SECONDARY SYPHILIS WITH UNUSUALLY SEVERE MANIFESTATIONS SIMULATING TERTIARY STAGE. Presented by DR. PAROUNAGIAN.

M. R., an Italian, aged 25, who presented himself at the Bellevue Syphilis Clinic on Dec. 1, 1924, gave the following history: Eight days after exposure, a sore appeared at the meatus, about three months ago, which was treated locally. Three weeks before presentation, he developed a sore throat, and an eruption appeared on the forehead, nose and lower extremities. The examination revealed extensive mucous patches in the throat, discrete papules and pustules on the forehead, alae nasi, nares, and upper lip, and scattered superficial gumma-like patches on the lower extremities. It was impossible to obtain any information as to a previous generalized roseola, since the lesions displayed represented a much later stage and unusual severity. A Wassermann test had been made, but the result had not yet been reported.

LICHEN PLANUS LINEARIS. Presented by DR. ROSEN.

A colored woman, aged 19, unmarried, who had been shown previously, presented a linear arrangement of papules, many of which were continuous from the left hand along the arm to and including the left shoulder blade; also two similar linear arrangements of papules on the right and left thigh and right knee. She had a gingivitis, as well as mucous patches on both lips. The Wassermann test was negative. Examination of the lesions of the lip for Vincent's organism was negative.

RADIODERMATITIS: PALMS AND FINGERS. Presented by DR. ABRAMOWITZ.

Mrs. Tillie F., from the Vanderbilt Clinic, an Austrian Jewess, aged 50, presented a skin disease of a year's duration. She said that one year ago she had received about twelve weekly roentgen-ray treatments for what, from her description, was a possible tinea of the palms, of five years' duration. She noticed that her hands, after slightly improving, became very dry and cracked, growing gradually worse, so that at the time of presentation there was a

marked keratosis of the palms with atrophy and telangiectases. The keratosis on the palmar aspect of the fingers was not so marked, but there was difficulty in closing the hands. On the left thenar eminence, the crusting was very thick, and bleeding was easily produced. In all probability, an epithelioma was present. The patient was referred for a plastic operation.

RAYNAUD'S DISEASE. Presented by DR. LEVIN.

R. R., a woman, unmarried, complained of a recurrent condition of the fingers of both hands. The condition was worse during the winter and cold weather, and after immersion in cold water. There were periods of improvement. She complained of itching, burning and intense pains. The toes of both feet had been affected for some time. The skin of the hands was purplish red and felt cold. This condition was more marked on the fingers, which were swollen, bluish red and cyanosed. The right index finger was beginning to show ulceration on the tip.

GUMMATOUS INFILTRATION OF THE STERNOMASTOID MUSCLE. Presented by DR. LEVIN.

E. C., a woman, married, aged 43, stated that for two months she had had a painful swelling on the left side of the neck. At times there were shooting pains radiating up toward the mastoid. Examination revealed a sausage-shaped hard mass running along the course of the left sternomastoid muscle. The Wassermann test proved to be four plus. Subsequent to one injection of arsphenamin and two of mercury, which she had received up to the time of presentation, the swelling diminished.

PAPULONECROTIC TUBERCULIDS ASSOCIATED WITH SARCOIDS. Presented by DR. ROSTENBERG.

Mrs. H. S., born in Russia, whose family history was irrelevant and who remembered having had typhoid fever ten years before, had a condition that started seven years ago, after coming to this country. Examination showed mainly that the forearms and breasts were involved, these locations presenting a large number of old and new scars varying from 0.25 to 2 cm. in diameter and a few new lesions in the form of subcutaneous reddish and purplish nodules of pinhead to pea size, some with necrotic tops. There were a few semicircular lesions on both breasts, consisting of a conglomeration of a number of reddish cutaneous and subcutaneous nodules, giving the appearance of a slightly elevated crest. A Wassermann test was negative; a Pirquet test was slightly positive.

CHRONIC HYDRARTHROSIS DUE TO CONGENITAL SYPHILIS. Presented by DR. ROSTENBERG.

P. C., aged 8 years, the second of five children, whose mother was suffering from a specific osteitis, had been well up to a year before presentation, when the present trouble started, both knees becoming involved. Examination revealed a marked distension with marked effusion and fluctuation, especially laterally, of both knees. The pain was not marked, nor was the motion greatly impaired; there was no grating and no discoloration of the skin. The roentgen-ray showed no destructive changes. The Wassermann test was four plus. Antisyphilitic treatment was only moderately successful.

OSCAR L. LEVIN, M.D., Secretary.

Book Reviews

INTRODUCTION TO DERMATOLOGY. By SIR NORMAN WALKER. Eighth edition. Eighth volume. Price, $7. Pp. 371, with 92 plates and 80 illustrations. New York: William Wood & Company, 1925.

It is necessary only to call attention to this new edition of Walker's "Dermatology." A work that has been a standard book for twenty-six years and that has gone through eight editions can claim the quality of old wine. Its character has long been known. Its author is a skilful dermatologist, with broad, general training, and he is a wise man. The book, accordingly, has character, and as a result has always been one of the interesting, original works on the subject. It has the great virtue of being reasonably compact. The colored illustrations, of which there are ninety-two, are excellent. Altogether it is a good book.

HANDBUCH DER SALVARSANTHERAPIE. Edited by DR. W. KOLLE and DR. K. ZIELER. Berlin and Vienna: Urban & Schwarzenberg, 1925.

The second volume of this monumental treatise on arsphenamin therapy has come to hand. It is necessary only to call the attention of syphilologists to its publication. It is an exhaustive treatise by experts, and a valuable reservoir of knowledge in this field.

Index to Current Literature

DERMATOLOGY

Abnormal Elasticity of Joints and Skin. A. Gilbert et al., Bull. et mém. Soc. méd. d. hôp. de Paris. **49**:307 (Feb. 27) 1925.

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